STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 202382

TO: Randall Winston
Location: rem/3D10/3C18
Art Unit: 1655
Friday, September 22, 2006
Case Serial Number: 10/790289

From: Les Henderson
Location: Biotech-Chem Library
REM-1A75
Phone: (571)272-2538

leslie.henderson@uspto.gov

Search Notes

Results can also be viewed via SCORE. http://es/ScoreAccessWeb/

A printed copy of your search results will be delivered to you later today AND an electronic copy of these same search results should be entered into SCORE as early as tomorrow.

STIC SEARCH RESULTS FEEDBACK FORM

Biotech-Chem Library

Questions about the scope or the results of the search? Contact ***the searcher or contact***:

Mary Hale, Information Branch Supervisor
571-272-2507 Remsen E01 D86

Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* ☐ *Example: 1610*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
  (journal articles, conference proceedings, new product announcements etc.)

- *Relevant prior art **not found:***
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC/Biotech-Chem Library Remsen Bldg.

9_1026

Access DB# 202382

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: RANDALL O'REAN WINSTON Examiner #: 78179 Date: 09/20/06

Art Unit: 1655 Phone Number 30 571-272-0972 Serial Number: 10/790,299

Mail Box and Bldg/Room Location: Remsen Results Format Preferred (circle): PAPER DISK E-MAIL

3C18 MailBox 3D10 Room number

MEY

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: PRODUCTS CONTAINING polyphenol(s) and L-Arginine and methods of use thereof

Inventors (please provide full names): KATI Achevaux -) See Attachment

Earliest Priority Filing Date: ~~03/12/1998~~ 03/12/1998

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Applicant Elected Claims 31-74.

Please Search the structure of claim 32. Thanks!!

STAFF USE ONLY

Searcher: _____

Searcher Phone #: _____

Type of Search

NA Sequence (#)_____

AA Sequence (#)_____

Vendors and cost where applicable

STN _____

Dialog _____

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=> d his ful

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                D SCAN
                SEL RN

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                OR 74-79-3/BI)
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                D SCAN
L4            1 SEA ABB=ON  PLU=ON  10102-43-9/RN
                D SCAN
L5            1 SEA ABB=ON  PLU=ON  125978-95-2/RN

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L11       123063 SEA ABB=ON  PLU=ON  L4 OR NITRIC(A)OXIDE
L12        34087 SEA ABB=ON  PLU=ON  L5 OR L11(A)SYNTHASE
L13          252 SEA ABB=ON  PLU=ON  L9 AND L10
L14           38 SEA ABB=ON  PLU=ON  L13 AND L11
                D SCAN L1
L15         2719 SEA ABB=ON  PLU=ON  L3/THU
L16            5 SEA ABB=ON  PLU=ON  L15 AND L14
                D SCAN
L17               QUE ABB=ON  PLU=ON  FOOD OR FEED
L18          639 SEA ABB=ON  PLU=ON  L9(L)L17
L19            1 SEA ABB=ON  PLU=ON  L18 AND L10 AND L11
                D SCAN
L20            3 SEA ABB=ON  PLU=ON  L14 AND L17
                D SCAN
L21               QUE ABB=ON  PLU=ON  CHOCOLAT? OR COCOA?
                E COCOA/CT
                E E3+ALL
L22         1538 SEA ABB=ON  PLU=ON  COCOA/CT
L23            0 SEA ABB=ON  PLU=ON  L14 AND L22
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L25          262 SEA ABB=ON  PLU=ON  L9 AND L21
L26           13 SEA ABB=ON  PLU=ON  L25 AND L10
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                D SCAN
L28           10 SEA ABB=ON  PLU=ON  L25 AND L11
                D SCAN
L29          103 SEA ABB=ON  PLU=ON  L9(L)L11
L30           14 SEA ABB=ON  PLU=ON  L29 AND L10
L31        15889 SEA ABB=ON  PLU=ON  L10(L)L11
L32           31 SEA ABB=ON  PLU=ON  L31 AND L9
L33           17 SEA ABB=ON  PLU=ON  L14 AND L12
L34           11 SEA ABB=ON  PLU=ON  L14 AND (POLYPHENOL? OR POLY(A)PHEN
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                OR L27 OR L28) OR L30 OR L34
L36           50 SEA ABB=ON  PLU=ON  L35 OR L33
                D 1-50 TI CC
L37          747 SEA ABB=ON  PLU=ON  L9 AND ?SACCHARID?
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                D SCAN
L39           50 SEA ABB=ON  PLU=ON  L38 OR L36
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                D 1-29 TI CC
L41           25 SEA ABB=ON  PLU=ON  L40 AND 1907-2004/PY,PRY
L42           13 SEA ABB=ON  PLU=ON  L14 NOT L41
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L43            7 SEA ABB=ON  PLU=ON  L42 AND 1907-2004/PY,PRY


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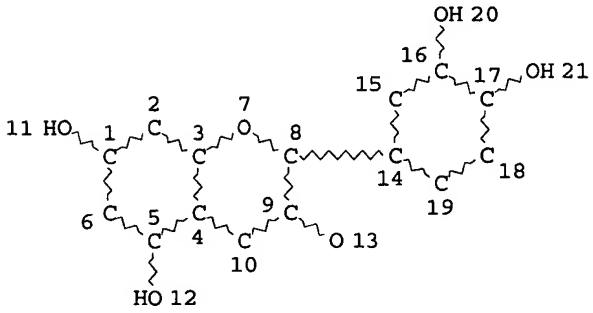


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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  21

STEREO ATTRIBUTES: NONE
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L9         32821 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8
L10        66809 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 OR L(A)ARGININE
L11       123063 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 OR NITRIC(A)OXIDE
L12        34087 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5 OR L11(A)SYNTHASE
L13          252 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND L10
L14           38 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13 AND L11
L15         2719 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3/THU
L16            5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L15 AND L14
L17               QUE  ABB=ON  PLU=ON  FOOD OR FEED
L18          639 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9(L)L17
L19            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L18 AND L10 AND L11
L20            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L14 AND L17
L21               QUE  ABB=ON  PLU=ON  CHOCOLAT? OR COCOA?
L24            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L14 AND L21
L25          262 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND L21
L26           13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L25 AND L10
L27            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L26 AND L11
L28           10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L25 AND L11
L29          103 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9(L)L11
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L30          14 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L29 AND L10
L33          17 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L14 AND L12
L34          11 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L14 AND (POLYPHENOL?
                OR POLY(A)PHENOL?)
L35          43 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 OR (L19 OR L20)
                OR L24 OR (L26 OR L27 OR L28) OR L30 OR L34
L36          50 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L35 OR L33
L37         747 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND ?SACCHARID?
L38           4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L37 AND L10 AND L11
L39          50 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L38 OR L36
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L41          25 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L40 AND 1907-2004/PY,P
                RY


=> d l41 1-25 ibib abs hitstr hitind

L41  ANSWER 1 OF 25  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:        2005:290535  HCAPLUS
DOCUMENT NUMBER:         142:456719
TITLE:                   Gastroprotective effect of L-
                         arginine and quercetin in
                         indomethacin-induced gastric lesions in rats
AUTHOR(S):               Abdallah, D. M.
CORPORATE SOURCE:        Department of Pharmacology & Toxicology,
                         Faculty of Pharmacy, Cairo University, Cairo,
                         Egypt
SOURCE:                  Egyptian Journal of Biomedical Sciences (
                         2004), 15, 194-206
                         CODEN: EJBSF3; ISSN: 1110-6379
PUBLISHER:               Egyptian Society for Biotechnology
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   The cytoprotective properties of L-arginine,
     the nitric oxide (NO) precursor, and quercetin
     an antioxidant natural flavonoid, in gastric mucosal injury
     induced by indomethacin has been investigated.  In this exptl.
     model the pathogenesis of the lesions has been related to production
     of reactive oxygen species and alterations in NO synthesis.  Thus,
     in this study, the antioxidant defense factors (glutathione,
     glutathione peroxidase, mucus, NO), the lesion-inducing effects of
     the generated oxygen free radicals (vascular permeability, lipid
     peroxidn.) and gastric ulceration (ulcer index) in Wistar rats
     treated orally with indomethacin (20 mg/kg) were examined L
     -arginine (300 mg/kg, p.o.) and quercetin (200 mg/kg,
     p.o.) were administered 1 h and 2 h, resp., prior to ulcer
     induction.  Both pretreatments produced antiulcerogenic activity
     associated with reduced lesive effects accompanied by increases in
     antioxidant defense factors.  However, quercetin did not alter
     mucus content significantly, as compared to indomethacin.
     Therefore, this study shows a cytoprotective effect of L
     -arginine and quercetin against indomethacin-induced
     ulceration.  This could be mediated by scavenging of oxygen
     derived free radicals and elevation of NO.
IT   10102-43-9, Nitric oxide, biological
     studies
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (L-arginine and quercetin exerted
        antiulcerogenic activity associated with increased antioxidant
        defense factors (glutathione, glutathione peroxidase, mucus,
        NO) in indomethacin-induced gastric lesion in rat model)
RN   10102-43-9  HCAPLUS
CN   Nitrogen oxide (NO) (8CI, 9CI)  (CA INDEX NAME)
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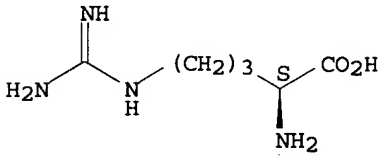
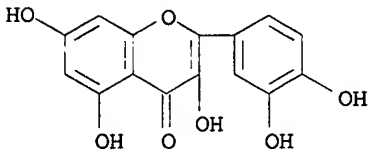
N═O

IT **74-79-3, L-Arginine**, biological studies
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(NO precursor **L-arginine** exerted antiulcerogenic activity linked with reduced lesive effects, increased antioxidant defense factor and may be mediated by scavenging of free radicals, NO elevation in indomethacin-induced gastric lesion in rat)
RN 74-79-3 HCAPLUS
CN L-Arginine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **117-39-5**, Quercetin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(flavonoid quercetin and **L-arginine** exerted antiulcerogenic activity linked with reduced lesive effect, raise antioxidant factor and may be mediated by free radical scavenging, NO elevation in indomethacin-induced gastric lesion in rat model)
RN 117-39-5 HCAPLUS
CN 4H-1-Benzopyran-4-one, 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy- (9CI) (CA INDEX NAME)



CC 1-9 (Pharmacology)
ST **L arginine** quercetin indomethacin gastric mucosa injury gastroprotectant
IT Lipid peroxidation
(**L-arginine** and quercetin exerted antiulcerogenic activity associated with reduced lesive effects of generated reactive oxygen species (vascular permeability and lipid peroxidn.) in indomethacin-induced gastric lesion in rat model)
IT Lipid peroxidation
Reactive oxygen species
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**L-arginine** and quercetin exerted antiulcerogenic activity associated with reduced lesive effects of generated reactive oxygen species (vascular permeability and lipid peroxidn.) in indomethacin-induced gastric lesion in rat model)
IT Mucus
(**L-arginine**, quercetin exerted

antiulcerogenic activity linked with increased antioxidant defense factors (glutathione, glutathione peroxidase, mucus, NO) and quercetin did not alter mucus in indomethacin-induced gastric lesion in rat model)

IT Flavonoids
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(flavonoid quercetin and **L-arginine** exerted antiulcerogenic activity linked with reduced lesive effect, raise antioxidant factor and may be mediated by free radical scavenging, NO elevation in indomethacin-induced gastric lesion in rat model)

IT Injury
(gastric mucosal; NO precursor **L-arginine** exerted antiulcerogenic activity linked with reduced lesive effects, increased antioxidant defense factor and may be mediated by scavenging of free radicals, NO elevation in indomethacin-induced gastric lesion in rat)

IT Cytoprotective agents
Gastrointestinal agents
(gastroprotective agents; **L-arginine** and quercetin showed cytoprotective effect against indomethacin-induced gastric lesion in rat model)

IT Stomach, disease
(mucosal injury; NO precursor **L-arginine** exerted antiulcerogenic activity linked with reduced lesive effects, increased antioxidant defense factor and may be mediated by scavenging of free radicals, NO elevation in indomethacin-induced gastric lesion in rat)

IT Blood vessel
(permeability; **L-arginine** and quercetin exerted antiulcerogenic activity associated with reduced lesive effects of generated reactive oxygen species (vascular permeability and lipid peroxidn.) in indomethacin-induced gastric lesion in rat model)

IT Stomach
(quercetin and **L-arginine** exerted antiulcerogenic activity linked with reduced lesive effect, raise antioxidant factor and may be mediated by free radical scavenging, NO elevation in indomethacin-induced gastric lesion in rat model)

IT 70-18-8, Glutathione, biological studies 9013-66-5, Glutathione peroxidase **10102-43-9**, **Nitric oxide**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**L-arginine** and quercetin exerted antiulcerogenic activity associated with increased antioxidant defense factors (glutathione, glutathione peroxidase, mucus, NO) in indomethacin-induced gastric lesion in rat model)

IT 7782-44-7D, Oxygen, reactive species
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**L-arginine** and quercetin exerted antiulcerogenic activity associated with reduced lesive effects of generated reactive oxygen species (vascular permeability and lipid peroxidn.) in indomethacin-induced gastric lesion in rat model)

IT **74-79-3**, **L-Arginine**, biological studies
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(NO precursor **L-arginine** exerted antiulcerogenic activity linked with reduced lesive effects, increased antioxidant defense factor and may be mediated by scavenging of free radicals, NO elevation in indomethacin-induced gastric lesion in rat)

IT **117-39-5**, Quercetin

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(flavonoid quercetin and **L-arginine** exerted antiulcerogenic activity linked with reduced lesive effect, raise antioxidant factor and may be mediated by free radical scavenging, NO elevation in indomethacin-induced gastric lesion in rat model)

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

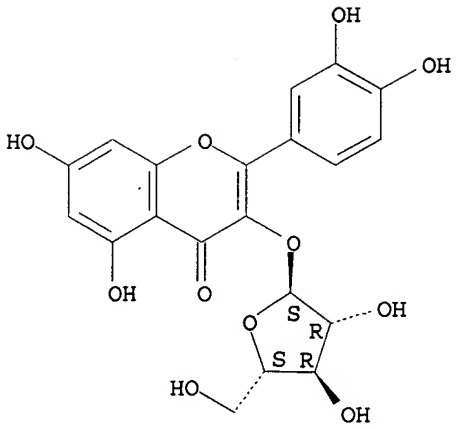
L41 ANSWER 2 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:539206 HCAPLUS
DOCUMENT NUMBER: 142:16743
TITLE: Inhibitory effects of flavonoids from Hypericum perforatum on **nitric oxide synthase**
AUTHOR(S): Luo, L.; Sun, Q.; Mao, Y. Y.; Lu, Y. H.; Tan, R. X.
CORPORATE SOURCE: Institute of Functional Biomolecules, State Key Laboratory of Pharmaceutical Biotechnology, Nanjing University, Nanjing, 210093, Peop. Rep. China
SOURCE: Journal of Ethnopharmacology (**2004**), 93(2-3), 221-225
CODEN: JOETD7; ISSN: 0378-8741
PUBLISHER: Elsevier Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The inhibitory effects of six flavonoids from Hypericum perforatum were assessed spectrophotometrically using **nitric oxide synthase** (NOS) in blood and cerebral homogenate of rats. Of the assayed compds., quercetin and hyperoside showed concentration-dependent enzyme inhibitory actions. The IC50 values of quercetin for inhibiting NOS in rat cerebral homogenate and blood were 63.06 and 57.54 μM, and those of hyperoside 56.23 and 158.49 μM, resp. The competitive patterns were discerned with the inhibition of the two flavonoids on NOS in serum and cerebral homogenate (except a mixed type inhibition was observed with quercetin in inhibiting cerebral NOS). Furthermore, similar inhibitions were found for quercetin upon NOS in cerebral homogenate and blood. However, a stronger inhibitory effect of hyperoside on the enzyme was discerned in cerebrum than in blood. These results suggested that the galactose moiety in hyperoside may be associated with the selectivity of the NOS inhibition.

IT **572-30-5P**, Avicularin
RL: NPO (Natural product occurrence); PAC (Pharmacological activity); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(flavonoid avicularin isolated from Hypericum perforatum was assayed for its inhibitory activity on **nitric oxide synthase** present in blood and cerebral homogenate of rat)

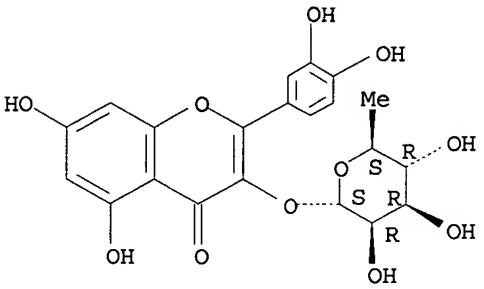
RN 572-30-5 HCAPLUS
CN 4H-1-Benzopyran-4-one, 3-(α-L-arabinofuranosyloxy)-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



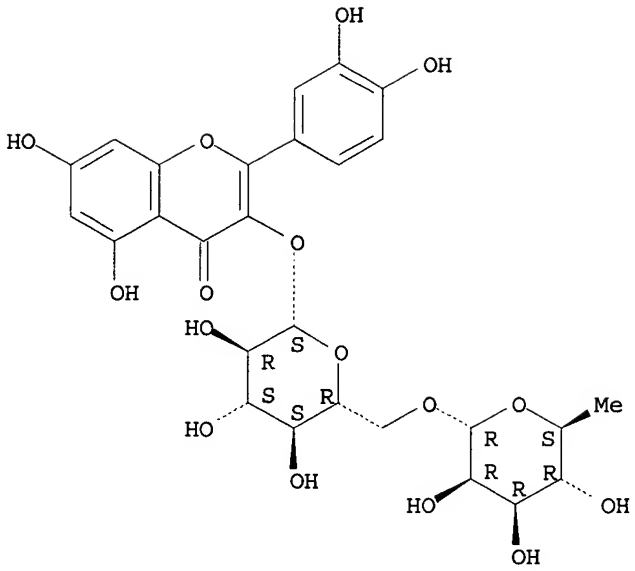
IT **522-12-3P**, Quercitrin
RL: NPO (Natural product occurrence); PAC (Pharmacological activity); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(flavonoid quercitrin isolated from Hypericum perforatum showed no inhibitory activity on **nitric oxide synthase** present in blood and cerebral homogenate of rat)
RN 522-12-3 HCAPLUS
CN 4H-1-Benzopyran-4-one, 3-[(6-deoxy-α-L-mannopyranosyl)oxy]-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **153-18-4P**, Rutin
RL: NPO (Natural product occurrence); PAC (Pharmacological activity); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(flavonoid rutin isolated from Hypericum perforatum showed no inhibitory activity on **nitric oxide synthase** present in blood and cerebral homogenate of rat)
RN 153-18-4 HCAPLUS
CN 4H-1-Benzopyran-4-one, 3-[[6-O-(6-deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy]-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-(9CI) (CA INDEX NAME)

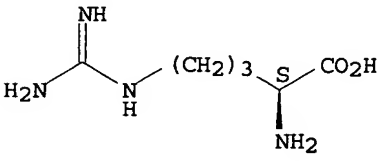
Absolute stereochemistry. Rotation (+).



IT **125978-95-2, Nitric oxide synthase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(flavonoids like quercetin and hyperoside isolated from Hypericum perforatum showed active inhibitory effect on **nitric oxide synthase** present in blood and cerebral homogenate of rat while quercitrin, rutin showed no activity)
RN 125978-95-2 HCAPLUS
CN Synthase, nitric oxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **74-79-3, L-Arginine**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(flavonoids quercetin and hyperoside isolated from Hypericum perforatum (St. John's wort) showed active inhibitory effect on **nitric oxide synthase** present in blood and cerebral homogenate of rat while quercitrin, rutin showed no activity)
RN 74-79-3 HCAPLUS
CN L-Arginine (9CI) (CA INDEX NAME)

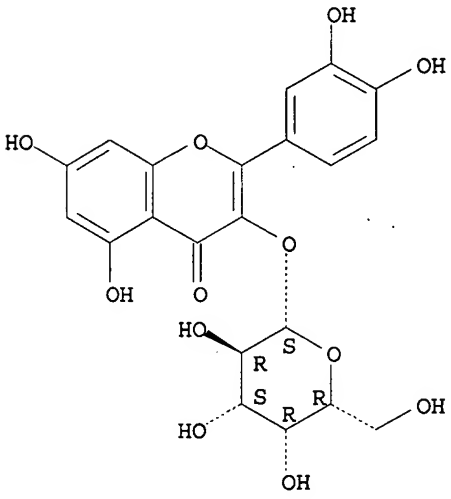
Absolute stereochemistry.



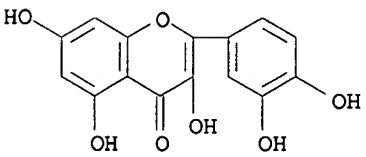
IT **482-36-0P**, Hyperoside
RL: NPO (Natural product occurrence); PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(hyperoside isolated from Hypericum perforatum showed potent competitive type inhibitory activity on NOS in blood and cerebral homogenate of rat with stronger inhibitory effect on

NOS in cerebrum than in blood)
RN 482-36-0 HCAPLUS
CN 4H-1-Benzopyran-4-one, 2-(3,4-dihydroxyphenyl)-3-β-D-galactopyranosyloxy)-5,7-dihydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **117-39-5P**, Quercetin
RL: NPO (Natural product occurrence); PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(quercetin isolated from Hypericum perforatum concentration-dependently, competitively inhibited rat blood NOS and showed mixed type inhibition in rat cerebral NOS without any difference in inhibitory potential between blood and cerebrum)
RN 117-39-5 HCAPLUS
CN 4H-1-Benzopyran-4-one, 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy- (9CI) (CA INDEX NAME)



CC 1-12 (Pharmacology)
ST flavonoid quercetin hyperoside Hypericum perforatum **nitric oxide synthase** antidepressant
IT Brain
(cerebrum; flavonoids quercetin showed mixed type inhibitory activity and hyperoside had competitive type inhibitory effect on **nitric oxide synthase** present in cerebral homogenate of rat)
IT Hypericum perforatum
(flavonoids like quercetin and hyperoside isolated from Hypericum perforatum showed active inhibitory effect on **nitric oxide synthase** present in blood and cerebral homogenate of rat while quercitrin, rutin showed no activity)
IT Blood
(flavonoids quercetin and hyperoside concentration-dependently and

competitively inhibited **nitric oxide synthase** present in blood of rat)

IT Natural products, pharmaceutical
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(flavonoids quercetin and hyperoside isolated from Hypericum perforatum (St. John's wort) showed active inhibitory effect on **nitric oxide synthase** present in blood and cerebral homogenate of rat while quercitrin, rutin showed no activity)

IT Antidepressants
(flavonoids quercetin and hyperoside with antidepressant activity, isolated from Hypericum perforatum showed active inhibitory effect on **nitric oxide synthase** present in blood and cerebral homogenate of rat)

IT Antioxidants
(flavonoids quercetin and hyperoside with antioxidant activity, isolated from Hypericum perforatum showed active inhibitory effect on **nitric oxide synthase** present in blood and cerebral homogenate of rat)

IT **572-30-5P**, Avicularin
RL: NPO (Natural product occurrence); PAC (Pharmacological activity); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(flavonoid avicularin isolated from Hypericum perforatum was assayed for its inhibitory activity on **nitric oxide synthase** present in blood and cerebral homogenate of rat)

IT 520-18-3P, Kaempferol
RL: NPO (Natural product occurrence); PAC (Pharmacological activity); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(flavonoid kaempferol isolated from Hypericum perforatum was assayed for its inhibitory activity on **nitric oxide synthase** present in blood and cerebral homogenate of rat)

IT **522-12-3P**, Quercitrin
RL: NPO (Natural product occurrence); PAC (Pharmacological activity); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(flavonoid quercitrin isolated from Hypericum perforatum showed no inhibitory activity on **nitric oxide synthase** present in blood and cerebral homogenate of rat)

IT **153-18-4P**, Rutin
RL: NPO (Natural product occurrence); PAC (Pharmacological activity); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(flavonoid rutin isolated from Hypericum perforatum showed no inhibitory activity on **nitric oxide synthase** present in blood and cerebral homogenate of rat)

IT **125978-95-2**, **Nitric oxide synthase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(flavonoids like quercetin and hyperoside isolated from Hypericum perforatum showed active inhibitory effect on **nitric oxide synthase** present in blood and cerebral homogenate of rat while quercitrin, rutin showed no activity)

IT **74-79-3**, **L-Arginine**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(flavonoids quercetin and hyperoside isolated from Hypericum perforatum (St. John's wort) showed active inhibitory effect on

nitric oxide synthase present in blood and cerebral homogenate of rat while quercitrin, rutin showed no activity)

IT **482-36-0P**, Hyperoside
RL: NPO (Natural product occurrence); PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(hyperoside isolated from Hypericum perforatum showed potent competitive type inhibitory activity on NOS in blood and cerebral homogenate of rat with stronger inhibitory effect on NOS in cerebrum than in blood)

IT **117-39-5P**, Quercetin
RL: NPO (Natural product occurrence); PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(quercetin isolated from Hypericum perforatum concentration-dependently, competitively inhibited rat blood NOS and showed mixed type inhibition in rat cerebral NOS without any difference in inhibitory potential between blood and cerebrum)

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:513526 HCAPLUS
DOCUMENT NUMBER: 141:47384
TITLE: Gastrointestinally deliverable formulation containing green tea extract and a **nitric oxide** donor for the reduction of postoperative complications
INVENTOR(S): Schneider, Heinz
PATENT ASSIGNEE(S): Fresenius Kabi Deutschland GmbH, Germany
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004052352	A1	20040624	WO 2003-EP12675	2003 1113

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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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WO 2003-EP12675 W
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AB The invention discloses a formulation, which can be administered gastrointestinally, containing green tea extract and at least one **nitric oxide** (NO) donor (or precursor thereof) which is a substrate of NO synthetase. The formulation is administered prior to surgical interventions, to eliminate or reduce the risk of postoperative complications.

IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study) (donors; gastrointestinally deliverable formulation containing green tea extract and **nitric oxide** donor for reduction of postoperative complications)

RN 10102-43-9 HCAPLUS
CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

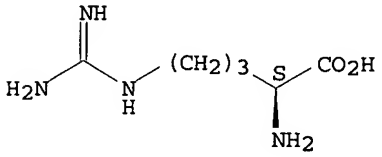
N═O

IT **125978-95-2**, **Nitric oxides synthase**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gastrointestinally deliverable formulation containing green tea extract and **nitric oxide** donor for reduction of postoperative complications)
RN 125978-95-2 HCAPLUS
CN Synthase, nitric oxide (9CI) (CA INDEX NAME)

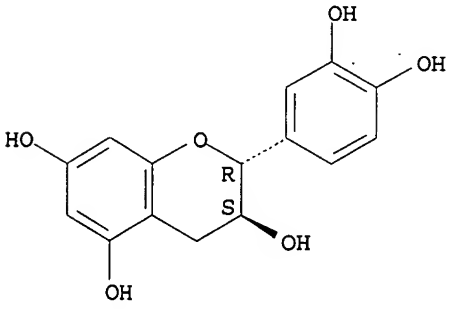
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **74-79-3**, **L-Arginine**, biological studies **154-23-4**, (+)-Catechin **154-23-4D**, Catechin, derivs. **490-46-0**, (-)-Epicatechin **970-73-0**, (+)-Gallocatechin **970-74-1**, (-)-Epigallocatechin **989-51-5**, (-)-Epigallocatechin gallate **1257-08-5**
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(gastrointestinally deliverable formulation containing green tea extract and **nitric oxide** donor for reduction of postoperative complications)
RN 74-79-3 HCAPLUS
CN L-Arginine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



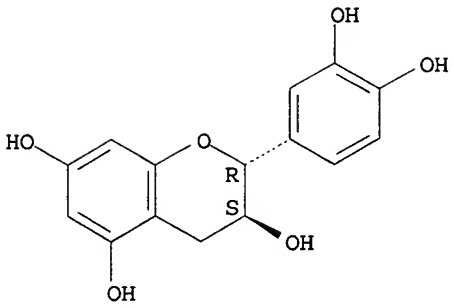
RN 154-23-4 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



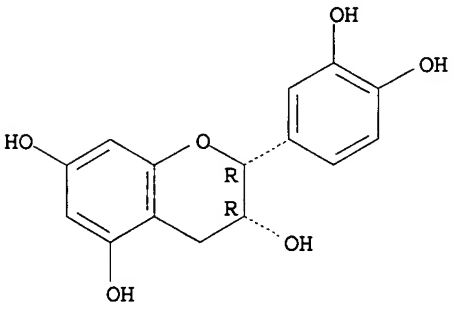
RN 154-23-4 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



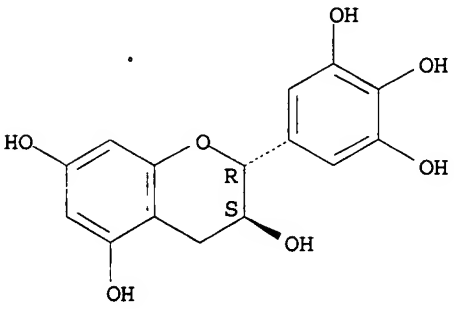
RN 490-46-0 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



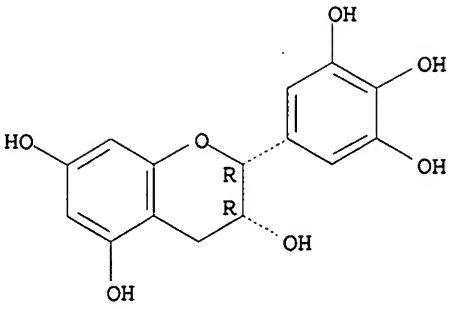
RN 970-73-0 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 3,4-dihydro-2-(3,4,5-trihydroxyphenyl)-, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



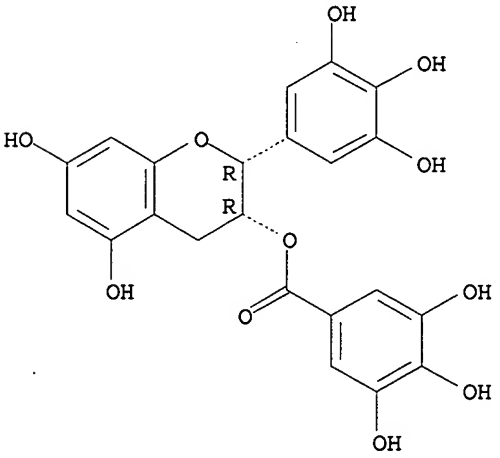
RN 970-74-1 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 3,4-dihydro-2-(3,4,5-trihydroxyphenyl)-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



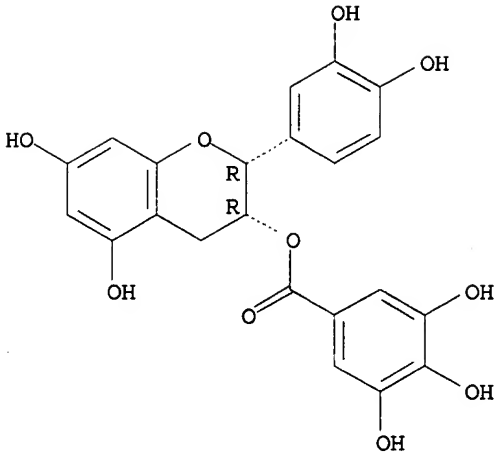
RN 989-51-5 HCAPLUS
CN Benzoic acid, 3,4,5-trihydroxy-, (2R,3R)-3,4-dihydro-5,7-dihydroxy-2-(3,4,5-trihydroxyphenyl)-2H-1-benzopyran-3-ylester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 1257-08-5 HCAPLUS
CN Benzoic acid, 3,4,5-trihydroxy-, (2R,3R)-2-(3,4-dihydroxyphenyl)-3,4-dihydro-5,7-dihydroxy-2H-1-benzopyran-3-ylester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IC ICM A61K031-04
ICS A61P041-00; A61K035-78; A61K031-198
CC 1-12 (Pharmacology)
IT Surgery
(cardiac; gastrointestinally deliverable formulation containing green tea extract and **nitric oxide** donor for reduction of postoperative complications)
IT Drug delivery systems
(gastrointestinal; gastrointestinally deliverable formulation containing green tea extract and **nitric oxide** donor for reduction of postoperative complications)
IT Anti-ischemic agents
Sepsis
Surgery
Transplant and Transplantation
(gastrointestinally deliverable formulation containing green tea extract and **nitric oxide** donor for reduction of postoperative complications)
IT Dipeptides
Tripeptides
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gastrointestinally deliverable formulation containing green tea extract and **nitric oxide** donor for reduction of postoperative complications)
IT Tea products
(green, extract of, green tea extract; gastrointestinally deliverable formulation containing green tea extract and **nitric oxide** donor for reduction of postoperative complications)
IT Ischemia
(hepatic; gastrointestinally deliverable formulation containing green tea extract and **nitric oxide** donor for reduction of postoperative complications)
IT Reperfusion
(injury; gastrointestinally deliverable formulation containing green tea extract and **nitric oxide** donor for reduction of postoperative complications)
IT Liver, disease
(ischemia; gastrointestinally deliverable formulation containing green tea extract and **nitric oxide** donor for reduction of postoperative complications)
IT Phenols, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**polyphenols**, nonpolymeric; gastrointestinally

deliverable formulation containing green tea extract and **nitric oxide** donor for reduction of postoperative complications)

IT Injury
(reperfusion; gastrointestinally deliverable formulation containing green tea extract and **nitric oxide** donor for reduction of postoperative complications)

IT Abdomen
Blood vessel
Digestive tract
Heart
Joint, anatomical
Nose
Pharynx
(surgery; gastrointestinally deliverable formulation containing green tea extract and **nitric oxide** donor for reduction of postoperative complications)

IT Injury
(trauma; gastrointestinally deliverable formulation containing green tea extract and **nitric oxide** donor for reduction of postoperative complications)

IT Surgery
(vascular; gastrointestinally deliverable formulation containing green tea extract and **nitric oxide** donor for reduction of postoperative complications)

IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(donors; gastrointestinally deliverable formulation containing green tea extract and **nitric oxide** donor for reduction of postoperative complications)

IT **125978-95-2**, **Nitric oxides synthase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gastrointestinally deliverable formulation containing green tea extract and **nitric oxide** donor for reduction of postoperative complications)

IT 55-63-0, Trinitroglycerin 56-40-6, Glycine, biological studies 56-85-9, L-Glutamine, biological studies **74-79-3**, **L-Arginine**, biological studies 79-17-4, Aminoguanidine 87-33-2, Isosorbide dinitrate **154-23-4**, (+)-Catechin **154-23-4D**, Catechin, derivs. **490-46-0**, (-)-Epicatechin **970-73-0**, (+)-Gallocatechin **970-74-1**, (-)-Epigallocatechin **989-51-5**, (-)-Epigallocatechin gallate **1257-08-5** 3081-61-6, Theanine 15078-28-1, Nitroprusside 33876-97-0, 3-Morpholinosydnonimine 136587-13-8 146724-96-1
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(gastrointestinally deliverable formulation containing green tea extract and **nitric oxide** donor for reduction of postoperative complications)

L41 ANSWER 4 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:114050 HCAPLUS
DOCUMENT NUMBER: 140:314762
TITLE: A Constituent of Green Tea, Epigallocatechin-3-gallate, Activates Endothelial **Nitric Oxide Synthase** by a Phosphatidylinositol-3-OH-kinase-, cAMP-dependent Protein Kinase-, and Akt-dependent Pathway and Leads to Endothelial-dependent Vasorelaxation
AUTHOR(S): Lorenz, Mario; Wessler, Silja; Follmann, Elena; Michaelis, Wanda; Duesterhoeft, Thomas; Baumann, Gert; Stangl, Karl; Stangl, Verena

CORPORATE SOURCE: Medizinische Klinik mit Schwerpunkt Kardiologie, Pneumologie, Angiologie, Charite, Humboldt-Universitaet zu Berlin, Berlin, D-10117, Germany
SOURCE: Journal of Biological Chemistry (**2004**), 279(7), 6190-6195
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

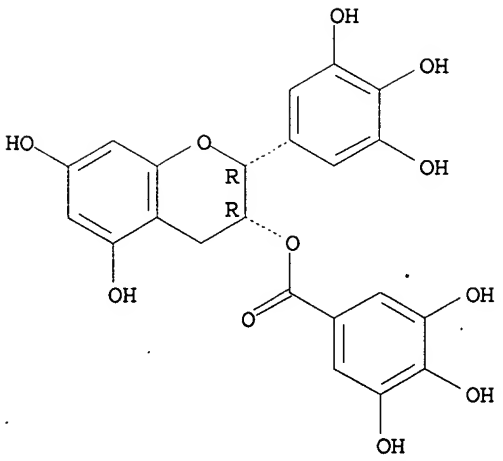
AB Epidemiol. studies suggest that tea catechins may reduce the risk of cardiovascular disease, but the mechanisms of benefit have not been determined The objective of the present study was to investigate the effects of epigallocatechin-3-gallate (EGCG), the major constituent of green tea, on vasorelaxation and on eNOS expression and activity in endothelial cells. EGCG (1-50 μM) induced dose-dependent vasodilation in rat aortic rings. Vasodilation was abolished by pretreatment with NG-nitro **L-arginine** Me ester. In bovine aortic endothelial cells, EGCG increased endothelial **nitric oxide** (eNOS) activity dose-dependently after 15 min. Treatment with EGCG induced a sustained activation of Akt, ERK1/2, and eNOS Ser1179 phosphorylation. Inhibition of extracellular signal-regulated kinase (ERK)1/2 had no influence on eNOS activity or Ser1179 phosphorylation. Simultaneous treatment of cells with selective inhibitors for cAMP-dependent protein kinase (PKA) and Akt completely prevented the increase in eNOS activity by EGCG after 15 min, indicating that both kinases act in concert. Specific phosphatidylinositol-3-OH-kinase inhibitors yielded identical results. Akt inhibition prevented eNOS Ser1179 phosphorylation, whereas inhibition of PKA did not influence Akt and eNOS Ser1179 phosphorylation. Pretreatment of endothelial cells with EGCG for 4 h markedly enhanced the increase in eNOS activity stimulated by Ca-ionomycin, suggesting that Akt accounts for prolonged eNOS activation. Treatment of cells for 72 h with EGCG did not change eNOS protein levels. Our results indicate that EGCG-induced endothelium-dependent vasodilation is primarily based on rapid activation of eNOS by a phosphatidylinositol 3-kinase-, PKA-, and Akt-dependent increase in eNOS activity, independently of an altered eNOS protein content.

IT **989-51-5**, Epigallocatechin-3-gallate
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(green tea constituent, epigallocatechin-3-gallate, activates eNOS by a phosphatidylinositol-3-kinase-, cAMP-dependent protein kinase-, and Akt-dependent pathway and leads to endothelial-dependent vasorelaxation)

RN 989-51-5 HCAPLUS

CN Benzoic acid, 3,4,5-trihydroxy-, (2R,3R)-3,4-dihydro-5,7-dihydroxy-2-(3,4,5-trihydroxyphenyl)-2H-1-benzopyran-3-ylester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



CC 1-8 (Pharmacology)
ST green tea epigallocatechin gallate **nitric oxide synthase** phosphatidylinositol kinase; vasodilator epigallocatechin gallate Akt kinase **nitric oxide synthase**
IT 115926-52-8, Phosphatidylinositol-3-kinase 137632-07-6, Protein kinase ERK1 137632-08-7, Protein kinase ERK2 142008-29-5, CAMP-dependent protein kinase 148640-14-6, Akt kinase 503473-02-7, Endothelial **nitric oxide synthase**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (green tea constituent, epigallocatechin-3-gallate, activates eNOS by a phosphatidylinositol-3-kinase-, cAMP-dependent protein kinase-, and Akt-dependent pathway and leads to endothelial-dependent vasorelaxation)
IT **989-51-5**, Epigallocatechin-3-gallate
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(green tea constituent, epigallocatechin-3-gallate, activates eNOS by a phosphatidylinositol-3-kinase-, cAMP-dependent protein kinase-, and Akt-dependent pathway and leads to endothelial-dependent vasorelaxation)
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 5 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:982471 HCAPLUS
DOCUMENT NUMBER: 140:228943
TITLE: Vasorelaxant effects of grape **polyphenols** in rat isolated aorta. Possible involvement of a purinergic pathway
AUTHOR(S): Mendes, Anne; Desgranges, Claude; Cheze, Catherine; Vercauteren, Joseph; Freslon, Jean-louis
CORPORATE SOURCE: Laboratoire de Pharmacodynamie, Faculte de Pharmacie, Universite Victor Segalen-Bordeaux 2, Bordeaux, Fr.
SOURCE: Fundamental & Clinical Pharmacology (**2003**), 17(6), 673-681
CODEN: FCPHEZ; ISSN: 0767-3981
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The purpose of this study was to investigate the mechanism of the vascular relaxation produced by **polyphenolic** substances from red wine, with a particular focus on the possible involvement of purinoceptors. With this aim, relaxing responses induced by procyanidin from grape seeds (GSP), anthocyanins, catechin and epicatechin were assessed in rat isolated aortic rings left intact (+E) or endothelium-denuded (-E). In prepns. precontracted with noradrenaline, incubation with NG-nitro-**L-arginine** Me ester (100 μM, 30 min) fully inhibited the GSP-induced relaxations. Concentration-effect curves to these substances (from 10-7 to 10-1 g/L) were determined in depolarized (60 mM KCl) prepns. in control condition, after incubation with reactive blue 2 (an antagonist of P2Y purinoceptors, 30 μM), with apyrase (an enzyme which hydrolyzes ATP and ADP, 0.8 U/mL) or with α,β-methylene ATP (an inhibitor of ecto ATPases, 10 μM). In (+E) rings, relaxations (expressed as percentage of initial contraction) were 41±2 and 37±3 for GSP and anthocyanins, resp. Only modest relaxations (10%) were observed in (-E) rings, as it was the case for catechin and epicatechin in (±E) rings. Reactive blue 2 or apyrase inhibited the GSP- and anthocyanin-induced relaxations in (+E) rings, while α,β-methylene ATP shifted to the left the relaxation curves obtained with GSP. These data confirm that modest relaxations observed with catechin and epicatechin are not endothelium-dependent but that GSP and anthocyanins induce a relaxing effect, which is related to the integrity of the endothelium and the synthesis and release of **nitric oxide** (NO). Furthermore, the inhibition by apyrase and the increase by ecto-ATPase inhibition of the GSP- and anthocyanin-induced relaxation suggest that these substances could act via an initial release of nucleotides, which in turn could activate P2Y1 and/or P2Y2 purinoceptors of endothelial cells, trigger the synthesis and release of NO and then lead to relaxation.

IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(vasorelaxant effects of grape **polyphenols** in rat isolated aorta. possible involvement of a purinergic pathway)

RN 10102-43-9 HCAPLUS

CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

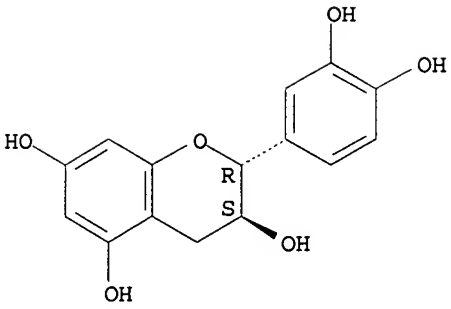
N═O

IT **154-23-4**, Catechin **490-46-0**, Epicatechin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vasorelaxant effects of grape **polyphenols** in rat isolated aorta. possible involvement of a purinergic pathway)

RN 154-23-4 HCAPLUS

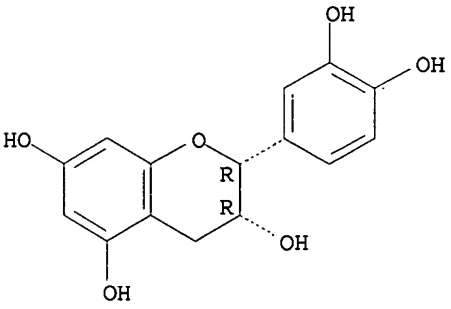
CN 2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 490-46-0 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



CC 1-8 (Pharmacology)
ST grape **polyphenol** vasorelaxant purinergic pathway
IT Purinoceptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(P2U; vasorelaxant effects of grape **polyphenols** in rat isolated aorta. possible involvement of a purinergic pathway)
IT Purinoceptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(P2Y; vasorelaxant effects of grape **polyphenols** in rat isolated aorta. possible involvement of a purinergic pathway)
IT Artery
(aorta; vasorelaxant effects of grape **polyphenols** in rat isolated aorta. possible involvement of a purinergic pathway)
IT Blood vessel
(endothelium; vasorelaxant effects of grape **polyphenols** in rat isolated aorta. possible involvement of a purinergic pathway)
IT Phenols, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**polyphenols**, nonpolymeric; vasorelaxant effects of grape **polyphenols** in rat isolated aorta. possible involvement of a purinergic pathway)
IT Nervous system
(purinergic; vasorelaxant effects of grape **polyphenols** in rat isolated aorta. possible involvement of a purinergic pathway)
IT Wine

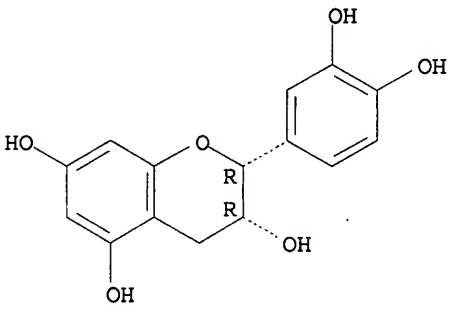
(red; vasorelaxant effects of grape **polyphenols** in rat isolated aorta. possible involvement of a purinergic pathway)
IT Endothelium
(vascular; vasorelaxant effects of grape **polyphenols** in rat isolated aorta. possible involvement of a purinergic pathway)
IT Vasodilators
Vitis vinifera
(vasorelaxant effects of grape **polyphenols** in rat isolated aorta. possible involvement of a purinergic pathway)
IT Anthocyanins
Procyanidins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vasorelaxant effects of grape **polyphenols** in rat isolated aorta. possible involvement of a purinergic pathway)
IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(vasorelaxant effects of grape **polyphenols** in rat isolated aorta. possible involvement of a purinergic pathway)
IT **154-23-4**, Catechin **490-46-0**, Epicatechin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vasorelaxant effects of grape **polyphenols** in rat isolated aorta. possible involvement of a purinergic pathway)
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 6 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:766792 HCAPLUS
DOCUMENT NUMBER: 140:41352
TITLE: Red wine **polyphenols** cause endothelium-dependent EDHF-mediated relaxations in porcine coronary arteries via a redox-sensitive mechanism
AUTHOR(S): Ndiaye, Mamadou; Chataigneau, Thierry; Andriantsitohaina, Ramaroson; Stoclet, Jean-Claude; Schini-Kerth, Valerie B.
CORPORATE SOURCE: Faculte de Pharmacie, Pharmacologie et Physico-Chimie des Interactions Cellulaires et Moleculaires, Universite Louis Pasteur de Strasbourg, Strasbourg, UMR CNRS 7034, Fr.
SOURCE: Biochemical and Biophysical Research Communications (**2003**), 310(2), 371-377
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Moderate consumption of wine is associated with cardiovascular protection most likely by increasing the endothelial formation of **nitric oxide** (NO). The present study investigated whether red wine **polyphenolic** compds. (RWPCs) increase the formation of endothelium-derived hyperpolarizing factor (EDHF) in arteries and, if so, to characterize the underlying mechanism. Porcine coronary artery rings were suspended in organ chambers for measurement of changes in isometric tension and membrane potential in the presence of indomethacin and Nω-nitro- **l-arginine**. RWPCs caused pronounced endothelium-dependent relaxations and hyperpolarizations, which were reduced by the combination of charybdotoxin plus apamin (two inhibitors of EDHF-mediated responses). Both responses to RWPCs were also reduced by

antioxidants, membrane permeant analogs of superoxide dismutase, and diphenylene iodonium, an inhibitor of flavin-dependent enzymes. RWPCs induced the formation of superoxide in cultured endothelial cells. These findings demonstrate that RWPCs cause EDHF-mediated relaxations of coronary arteries, which are critically dependent on a redox-sensitive mechanism involving a flavin-dependent enzyme.

IT **490-46-0**, Epicatechin
RL: BSU (Biological study, unclassified); NPO (Natural product occurrence); BIOL (Biological study); OCCU (Occurrence)
(dimers B1 and B2; red wine **polyphenols** cause endothelium-dependent EDHF-mediated relaxations in porcine coronary arteries via a redox-sensitive mechanism)
RN 490-46-0 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

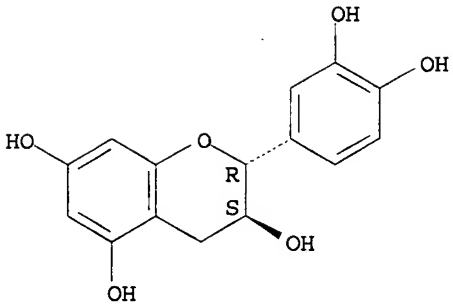


IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(red wine **polyphenols** cause endothelium-dependent EDHF-mediated relaxations in porcine coronary arteries via a redox-sensitive mechanism)
RN 10102-43-9 HCAPLUS
CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

N═O

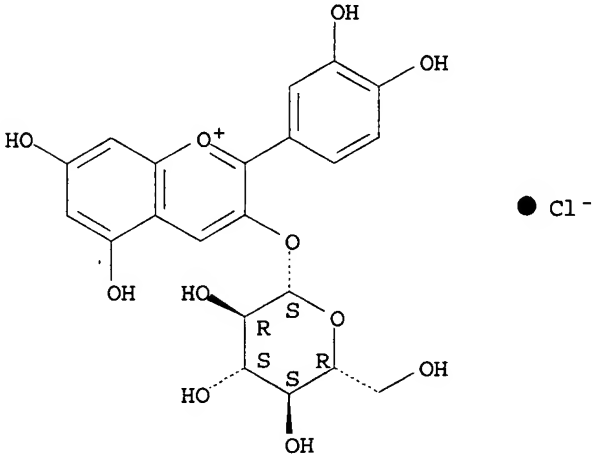
IT **154-23-4**, Catechin **7084-24-4**, Cyanidin-3-glucoside
RL: BSU (Biological study, unclassified); NPO (Natural product occurrence); BIOL (Biological study); OCCU (Occurrence)
(red wine **polyphenols** cause endothelium-dependent EDHF-mediated relaxations in porcine coronary arteries via a redox-sensitive mechanism)
RN 154-23-4 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 7084-24-4 HCAPLUS
CN 1-Benzopyrylium, 2-(3,4-dihydroxyphenyl)-3-β-D-glucopyranosyloxy)-5,7-dihydroxy-, chloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 18-7 (Animal Nutrition)
Section cross-reference(s): 1, 17
ST red wine **polyphenol** antioxidant endothelium hyperpolarizing factor coronary vasodilation
IT Phenols, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**polyphenols**, nonpolymeric; red wine **polyphenols** cause endothelium-dependent EDHF-mediated relaxations in porcine coronary arteries via a redox-sensitive mechanism)
IT Dietary supplements
Vasodilation
(red wine **polyphenols** cause endothelium-dependent EDHF-mediated relaxations in porcine coronary arteries via a redox-sensitive mechanism)
IT Reactive oxygen species
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(red wine **polyphenols** cause endothelium-dependent EDHF-mediated relaxations in porcine coronary arteries via a redox-sensitive mechanism)
IT Wine
(red; red wine **polyphenols** cause endothelium-dependent EDHF-mediated relaxations in porcine coronary arteries via a redox-sensitive mechanism)
IT **490-46-0**, Epicatechin

RL: BSU (Biological study, unclassified); NPO (Natural product occurrence); BIOL (Biological study); OCCU (Occurrence)
(dimers B1 and B2; red wine **polyphenols** cause endothelium-dependent EDHF-mediated relaxations in porcine coronary arteries via a redox-sensitive mechanism)

IT 7782-44-7D, Oxygen, reactive species 9002-17-9, Xanthine oxidase 9032-22-8, NADPH oxidase 9035-51-2, Cytochrome P 450, biological studies 9054-89-1, Superoxide dismutase **10102-43-9**, **Nitric oxide**, biological studies 11062-77-4, Superoxide 116788-37-5, Endothelium-derived hyperpolarizing factor 503473-02-7, Endothelial **nitric oxide synthase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(red wine **polyphenols** cause endothelium-dependent EDHF-mediated relaxations in porcine coronary arteries via a redox-sensitive mechanism)

IT 149-91-7, Gallic acid, biological studies **154-23-4**, Catechin 331-39-5, Caffeic acid 6906-39-4, Peonidin-3-glucoside **7084-24-4**, Cyanidin-3-glucoside 7228-78-6, Malvidin-3-glucoside 67879-58-7, Caftaric acid
RL: BSU (Biological study, unclassified); NPO (Natural product occurrence); BIOL (Biological study); OCCU (Occurrence)
(red wine **polyphenols** cause endothelium-dependent EDHF-mediated relaxations in porcine coronary arteries via a redox-sensitive mechanism)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 7 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:732952 HCAPLUS
DOCUMENT NUMBER: 140:246739
TITLE: Possible mechanisms of action in quercetin reversal of morphine tolerance and dependence
AUTHOR(S): Naidu, Pattipati; Singh, Amanpreet; Joshi, Dipesh; Kulkarni, Shrinivas
CORPORATE SOURCE: Pharmacol. Div., Univ. Inst. Pharmaceutical Sci., Panjab Univ., Chandigarh, India
SOURCE: Addiction Biology (2003), 8(3), 327-336
CODEN: ADBIFN; ISSN: 1355-6215
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In an earlier study, the authors reported the ability of quercetin to reverse the development of morphine tolerance and dependence in mice. In the present study the authors have attempted to explore the possible involvement of **nitric oxide** (NO) system in quercetin reversal of morphine tolerance and dependence in mice. Co-administration of L-NG-nitro arginine Me ester (L-NAME) or quercetin with morphine during induction phase (days 1-9) delayed the development of tolerance to the antinociceptive action of morphine and also reversed naloxone precipitated withdrawal jumps. **L-Arginine** administration during the induction phase enhanced the development of tolerance to the antinociceptive effect of morphine but had no effect on the naloxone-precipitated withdrawal jumps. During the expression phase (day 10) acute administration of quercetin or L-NAME reversed, whereas **L-arginine** facilitated naloxone-precipitated withdrawal jumps in morphine-tolerant mice, but none of these drugs affected the nociceptive threshold in withdrawal jumps in morphine-tolerant mice, but none of these drugs affected the nociceptive threshold in morphine-tolerant mice. Further, co-administration of quercetin or L-NAME with **L-arginine** during the induction phase antagonized the latter effects on the development of morphine tolerance. Also, prior administration of quercetin or

L-NAME reversed the **L-arginine** potentiation of naloxone-precipitated withdrawal jumps in morphine tolerance and dependence may involve its ability to support **nitric oxide synthase** (NOS) activity.

IT **10102-43-9, Nitric oxide**, biological studies **125978-95-2, Nitric oxide synthase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(possible mechanisms of action in quercetin reversal of morphine tolerance and dependence)

RN 10102-43-9 HCAPLUS
CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

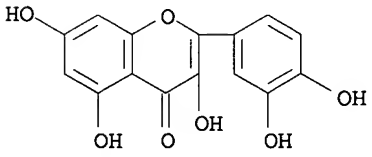
N═O

RN 125978-95-2 HCAPLUS
CN Synthase, nitric oxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **117-39-5**, Quercetin
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(possible mechanisms of action in quercetin reversal of morphine tolerance and dependence)

RN 117-39-5 HCAPLUS
CN 4H-1-Benzopyran-4-one, 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy- (9CI) (CA INDEX NAME)



CC 1-11 (Pharmacology)
ST quercetin morphine tolerance dependence **nitric oxide**

IT **10102-43-9, Nitric oxide**, biological studies **125978-95-2, Nitric oxide synthase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(possible mechanisms of action in quercetin reversal of morphine tolerance and dependence)

IT **117-39-5**, Quercetin
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(possible mechanisms of action in quercetin reversal of morphine tolerance and dependence)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:355610 HCAPLUS
DOCUMENT NUMBER: 138:348714
TITLE: Use of peroxynitrite scavengers or peroxynitrite formation inhibitors that do not diminish **nitric oxide** synthesis or activity to reverse or prevent

premature vascular senescence
INVENTOR(S): Goligorsky, Michael S.; Chen, Jun
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003086916	A1	20030508	US 2002-269032	2002 1011 <--
US 2005113427	A1	20050526	US 2004-13457	2004 1217 <--

PRIORITY APPLN. INFO.: US 2001-329010P P 2001 1012 <--
US 2002-269032 A1 2002 1011 <--

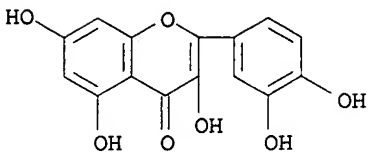
AB Premature vascular senescence is reversed or prevented in tissue or cells by contacting the tissue or cells with a peroxynitrite scavenger or peroxynitrite formation inhibitor that does not diminish **nitric oxide** synthesis. This finds application in treatment of patients with a disorder associated with elevated levels of advanced glycation end products in blood or tissue, e.g., patients with end stage renal disease or poorly controlled diabetes, and in contacting vascular tissue or cells ex vivo to prevent occurrence of premature senescence. Human umbilical vein endothelial cells (HUVEC) after four passages were plated on glycated collagen with or without the addition of 0.1 mM ebselen. Ebselen was able to reverse premature senescence at all dilns. of glycated collagen.

IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)
RN 10102-43-9 HCAPLUS
CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

N═O

IT **117-39-5**, Quercetin
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)
RN 117-39-5 HCAPLUS
CN 4H-1-Benzopyran-4-one, 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-

(9CI) (CA INDEX NAME)



IC ICM A61K038-44
ICS A61K031-555; A61K031-445; A61K031-416; A61K031-353; A61K031-198; A61K031-192; A61K035-78
INCL 424094400; 514185000; 514410000; 514327000; 514407000; 514456000; 514561000; 424769000; 514569000; 514562000
CC 1-8 (Pharmacology)
Section cross-reference(s): 9
IT Glycoproteins
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(AGE (advanced glycosylation end product), treatment of patients with; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)
IT Animal cell line
(HUVEC, ebselen reversal of premature senescence of; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)
IT Transplant and Transplantation
(allotransplant, treatment of cells or tissue seeded onto; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)
IT Artery
Blood vessel
(artificial, treatment of cells or tissue seeded onto; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)
IT Kidney, disease
(chronic, treatment of; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)
IT Nervous system, disease
(degeneration, treatment of; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)
IT Kidney, disease
(failure, chronic, irreversible, treatment of; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)
IT Drug delivery systems
(liposomes, cationic, with entrapped superoxide dismutase; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular

senescence)
IT Radical scavengers
(of peroxynitrite; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)
IT Blood vessel, disease
(peripheral, treatment of; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)
IT Animal tissue culture
Animals
Anti-Alzheimer's agents
Antidiabetic agents
Human
(peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)
IT Flavonoids
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)
IT Carboxylic acids, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phenolic; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)
IT Embryophyta
Plants
(**polyphenols** of; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)
IT Phenols, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**polyphenols**, nonpolymeric; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)
IT Blood vessel, disease
(premature senescence; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)
IT Cell aging
(premature vascular; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)
IT Polyoxyalkylenes, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reaction products with superoxide dismutase; peroxynitrite scavengers or peroxynitrite formation inhibitors not

diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)

IT Medical goods
(stents, treatment of cells or tissue seeded onto; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)

IT Lupus erythematosus
(systemic, treatment of; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)

IT Animal tissue
Blood
(treatment of patients with advanced glycation end products in; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)

IT Diabetes mellitus
(treatment of poorly controlled; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)

IT Alzheimer's disease
(treatment of; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)

IT Heart
(valve, artificial, treatment of cells or tissue seeded onto; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)

IT Transplant and Transplantation
(xenotransplant, treatment of cells or tissue seeded onto; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)

IT 469-32-9, Hamamelitannin
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bark exts. containing; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)

IT 9054-89-1D, C-terminal glycine and arginine tail-containing
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(copper-zinc-containing; peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)

IT 19059-14-4, Peroxynitrite
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)

IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)

IT 52-90-4D, L-Cysteine, substituted with tellurium or selenium 56-89-3D, L-Cystine, substituted with tellurium or selenium 63-68-3D, Methionine, substituted with tellurium or selenium 69-93-2, Uric acid, biological studies 89-25-8, 3-Methyl-1-phenyl-2-pyrazolin-5-one 94-93-9D, Salen, manganese complexes 101-60-0D, Porphyrin, manganese complexes **117-39-5**, Quercetin 124-09-4D, Hexamethylenediamine, conjugates with superoxide dismutase 327-97-9, Chlorogenic acid 331-39-5, Caffeic acid 530-59-6, Sinapic acid 635-78-9, Resorufin 1135-24-6, Ferulic acid 2226-96-2 7782-49-2D, Selenium, cystine or cysteine or methionine compds. 9054-89-1D, Superoxide dismutase, conjugates with hexamethylenediamine or reaction products with PEG 13494-80-9D, Tellurium, cystine or cysteine or methionine compds. 16397-91-4D, Manganese II, complexes with bis(cyclohexylpyridine)-substitutedmacrocyclic ligand, biological studies 25322-68-3D, Polyethylene glycol, reaction products with superoxide dismutase 53054-07-2, Nω-Hydroxy- **L-arginine** 55266-18-7 60489-13-6, 5,10,15,20-Tetrakis(N-methyl-4'-pyridyl)porphyrinato iron (III) 60940-34-3, Ebselen 139028-97-0, 5,10,15,20-Tetrakis(2,4,6-trimethyl-3,5-disulfonatophenyl)porphyrinato iron (III) 223723-79-3 256474-80-3
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peroxynitrite scavengers or peroxynitrite formation inhibitors not diminishing **nitric oxide** synthesis or activity for reversing or preventing premature vascular senescence)

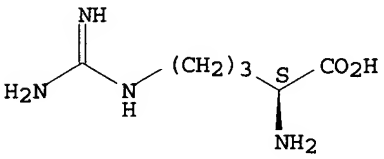
L41 ANSWER 9 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:199651 HCAPLUS
DOCUMENT NUMBER: 138:348662
TITLE: Influence of Green Tea **Polyphenol** in Rats with Arginine-Induced Renal Failure
AUTHOR(S): Yokozawa, Takako; Cho, Eun Ju; Nakagawa, Takako
CORPORATE SOURCE: Institute of Natural Medicine, Toyama Medical and Pharmaceutical University, Toyama, 930-0194, Japan
SOURCE: Journal of Agricultural and Food Chemistry (**2003**), 51(8), 2421-2425
CODEN: JAFCAU; ISSN: 0021-8561
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To determine whether green tea **polyphenol** ameliorates the pathol. conditions induced by excessive dietary arginine, green tea **polyphenol** was administered to rats at a daily dose of 50 or 100 mg/kg body weight for 30 days with a 2% weight/weight arginine diet. In arginine-fed control rats, urinary and/or serum levels of guanidino compds., **nitric oxide** (NO), urea, protein, and glucose increased significantly, while the renal activities of the oxygen species-scavenging enzymes superoxide dismutase (SOD) and catalase decreased, compared with casein-fed rats. However, rats given green tea **polyphenol** showed significant and dose-dependent decreases in serum levels of creatinine (Cr) and urea nitrogen and urinary excretion of Cr, and

they exerted a slight reduction of nitrite plus nitrate, indicating that green tea **polyphenol** reduced the production of uremic toxins and NO. In addition, in arginine-fed rats the urinary urea, protein, and glucose level increases were reversed by the administration of green tea **polyphenol**. Moreover, in rats given green tea **polyphenol** the SOD and catalase activities suppressed by excessive arginine administration increased dose-dependently, implying the biol. defense system was augmented as a result of free radical scavenging. These results suggest that green tea **polyphenol** would ameliorate renal failure induced by excessive dietary arginine by decreasing uremic toxin, and NO production and increasing radical-scavenging enzyme activity.

IT **74-79-3**, Arginine, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(green tea **polyphenol** effect on excessive dietary arginine-induced renal failure)
RN 74-79-3 HCAPLUS
CN L-Arginine (9CI) (CA INDEX NAME)

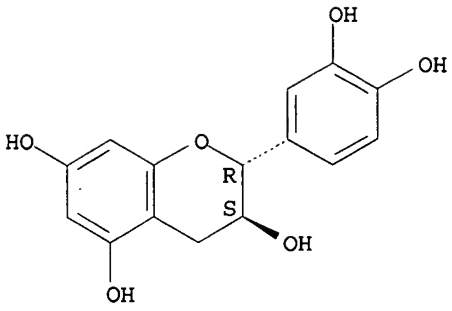
Absolute stereochemistry.



IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(green tea **polyphenol** effect on excessive dietary arginine-induced renal failure)
RN 10102-43-9 HCAPLUS
CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

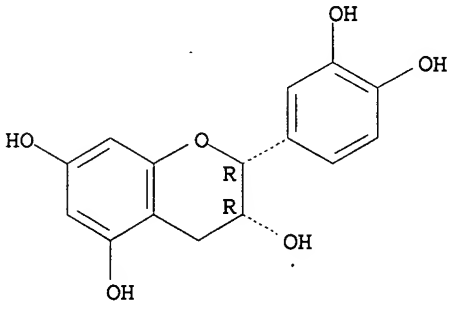
IT **154-23-4**, (+)-Catechin **490-46-0**, (-)-Epicatechin **970-73-0**, (+)-Gallocatechin **970-74-1**, (-)-Epigallocatechin **989-51-5**, (-)-Epigallocatechin 3-O-gallate **1257-08-5**, (-)-Epicatechin 3-O-gallate **4233-96-9**, (-)-Gallocatechin 3-O-gallate
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(green tea **polyphenol** effect on excessive dietary arginine-induced renal failure)
RN 154-23-4 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



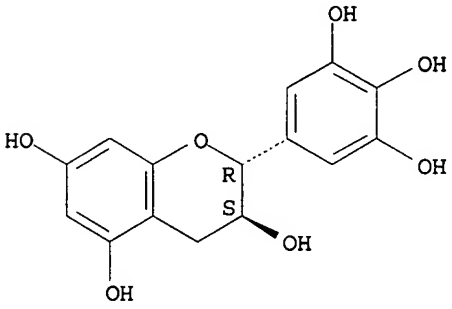
RN 490-46-0 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



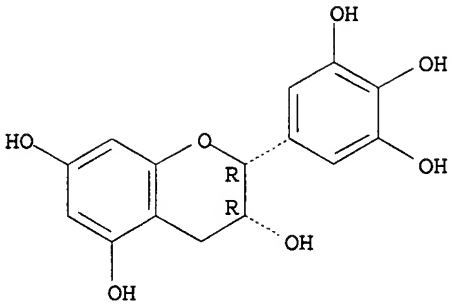
RN 970-73-0 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 3,4-dihydro-2-(3,4,5-trihydroxyphenyl)-, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



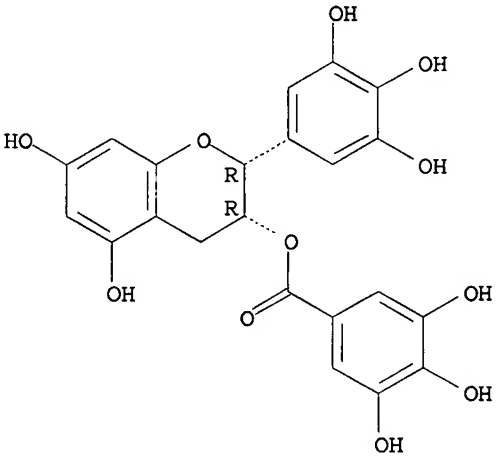
RN 970-74-1 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 3,4-dihydro-2-(3,4,5-trihydroxyphenyl)-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



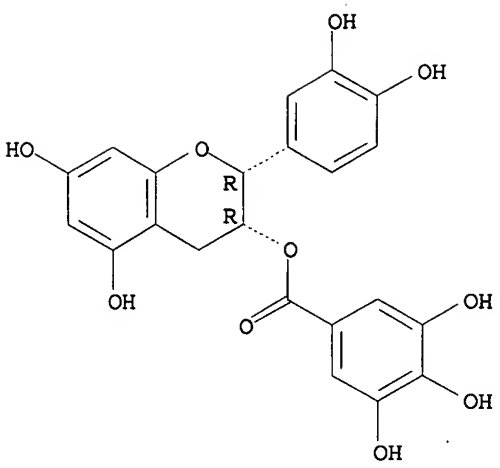
RN 989-51-5 HCAPLUS
CN Benzoic acid, 3,4,5-trihydroxy-, (2R,3R)-3,4-dihydro-5,7-dihydroxy-2-(3,4,5-trihydroxyphenyl)-2H-1-benzopyran-3-ylester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



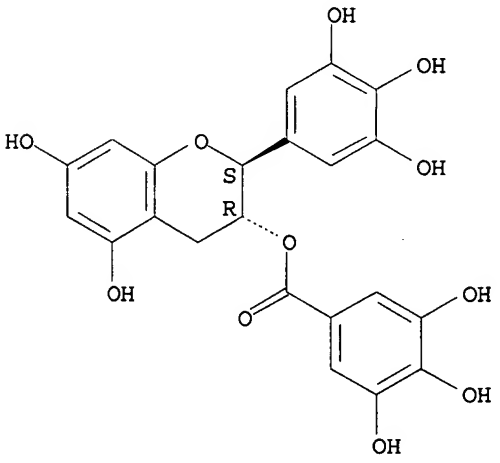
RN 1257-08-5 HCAPLUS
CN Benzoic acid, 3,4,5-trihydroxy-, (2R,3R)-2-(3,4-dihydroxyphenyl)-3,4-dihydro-5,7-dihydroxy-2H-1-benzopyran-3-ylester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 4233-96-9 HCAPLUS
CN Benzoic acid, 3,4,5-trihydroxy-, (2S,3R)-3,4-dihydro-5,7-dihydroxy-2-(3,4,5-trihydroxyphenyl)-2H-1-benzopyran-3-ylester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



CC 1-12 (Pharmacology)
ST green tea **polyphenol** radical scavenger dietary arginine renal failure
IT Kidney, disease
(failure; green tea **polyphenol** effect on excessive dietary arginine-induced renal failure)
IT Antioxidants
Dietary supplements
Radical scavengers
Tea products
(green tea **polyphenol** effect on excessive dietary arginine-induced renal failure)
IT Reactive oxygen species
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(green tea **polyphenol** effect on excessive dietary arginine-induced renal failure)
IT Phenols, biological studies
RL: DMA (Drug mechanism of action); PAC (Pharmacological

activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**polyphenols**, nonpolymeric; green tea **polyphenol** effect on excessive dietary arginine-induced renal failure)
IT Cytoprotective agents
(renal; green tea **polyphenol** effect on excessive dietary arginine-induced renal failure)
IT **74-79-3**, Arginine, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(green tea **polyphenol** effect on excessive dietary arginine-induced renal failure)
IT 7782-44-7D, Oxygen, reactive species 9001-05-2, Catalase 9054-89-1, Superoxide dismutase **10102-43-9**, **Nitric oxide**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(green tea **polyphenol** effect on excessive dietary arginine-induced renal failure)
IT **154-23-4**, (+)-Catechin **490-46-0**, (-)-Epicatechin **970-73-0**, (+)-Gallocatechin **970-74-1**, (-)-Epigallocatechin **989-51-5**, (-)-Epigallocatechin 3-O-gallate **1257-08-5**, (-)-Epicatechin 3-O-gallate **4233-96-9**, (-)-Gallocatechin 3-O-gallate
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(green tea **polyphenol** effect on excessive dietary arginine-induced renal failure)
IT 57-13-6, Urea, biological studies 60-27-5, Creatinine 471-29-4, Methylguanidine 6133-30-8, Guanidinosuccinic acid
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(uremic toxin; green tea **polyphenol** effect on excessive dietary arginine-induced renal failure)
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:164483 HCAPLUS
DOCUMENT NUMBER: 138:400661
TITLE: Synergistic suppression of superoxide and **nitric oxide** generation from inflammatory cells by combined **food** factors
AUTHOR(S): Murakami, Akira; Takahashi, Daisuke; Koshimizu, Koichi; Ohigashi, Hajime
CORPORATE SOURCE: Graduate School of Agriculture, Division of Food Science and Biotechnology, Kyoto University, Kyoto, 606-8502, Japan
SOURCE: Mutation Research (**2003**), 523-524, 151-161
CODEN: MUREAV; ISSN: 0027-5107
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In contrast to chemopreventive strategies using individual agents, a combination of specified compds. may be effectual to achieve desirable results with higher efficacy and lower toxicity. In the present in vitro study, the authors examined combinations of agents and assessed which concns. were appropriate to yield notable synergism. L-NG-Monomethyl-L-**arginine** (**L-NMMA**), a synthetic inducible **nitric oxide synthase** (iNOS) inhibitor, and zerumbone, a natural sesquiterpene that suppresses iNOS de novo synthesis, were combined at various concns., with the aim to diminish

combined **lipopolysaccharide**- and interferon-γ-induced **nitric oxide** generation in a murine macrophage line, RAW264.7. Although the combinatorial effects (CEs) were antagonistic or additive at higher concns., significant synergism was obtained at lower concns. where each agent alone did not cause significant inhibition. Similarly, the CEs were synergistic when (-)-epigallocatechin gallate (EGCG) and genistein were combined at lower concns., whereas those of two iNOS inhibitors, L-NMMA and L-NG-aminoethyl-L-ornithine, were either additive or antagonistic at all concns. tested, suggesting that a combination of given agents with different action mechanisms is a prerequisite for synergistic effects. For suppression of phorbol ester-induced superoxide anion radical (O2•-) generation in differentiated HL-60 cells, the CEs of 1'-acetoxychavicol acetate (ACA), a Ph propanoid that suppresses O2•- generation, and O2•- dismutase were also synergistic, though only at lower concns. The CEs of ACA/EGCG were antagonistic or additive, even at low concns., suggesting that the signal transduction pathways triggered by these agents are antagonistic. The present findings suggest that individual **food** phytochems. have complex interactions that can be antagonistic, additive, and/or synergistic in biol. systems, depending upon certain environmental factors including concns. Further, these results support and emphasize the concept that combinations of different types of chems. at low concns. are one of the essential areas of study for chemopreventive strategies.

IT **10102-43-9**, **Nitric oxide**, biological studies
RL: ADV (Adverse effect, including toxicity); FMU (Formation, unclassified); BIOL (Biological study); FORM (Formation, nonpreparative)
(synergistic suppression of superoxide and **nitric oxide** generation from inflammatory cells by combined **food** factors)

RN 10102-43-9 HCAPLUS

CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

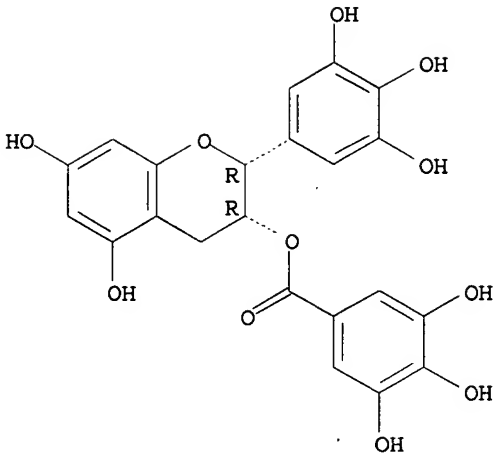
N═O

IT **989-51-5**, (-)-Epigallocatechin gallate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(synergistic suppression of superoxide and **nitric oxide** generation from inflammatory cells by combined **food** factors)

RN 989-51-5 HCAPLUS

CN Benzoic acid, 3,4,5-trihydroxy-, (2R,3R)-3,4-dihydro-5,7-dihydroxy-2-(3,4,5-trihydroxyphenyl)-2H-1-benzopyran-3-ylester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



CC 17-5 (Food and Feed Chemistry)
Section cross-reference(s): 4
ST antioxidant superoxide **nitric oxide** radical scavenger
IT Antioxidants
Human
(synergistic suppression of superoxide and **nitric oxide** generation from inflammatory cells by combined **food** factors)
IT **10102-43-9**, **Nitric oxide**, biological studies 11062-77-4, Superoxide
RL: ADV (Adverse effect, including toxicity); FMU (Formation, unclassified); BIOL (Biological study); FORM (Formation, nonpreparative)
(synergistic suppression of superoxide and **nitric oxide** generation from inflammatory cells by combined **food** factors)
IT 331-39-5, Caffeic acid 446-72-0, Genistein 471-05-6, Zerumbone 501-36-0, Resveratrol 622-78-6, Benzylisothiocyanate **989-51-5**, (-)-Epigallocatechin gallate 9054-89-1, Superoxide dismutase 17035-90-4 52946-22-2, 1'-Acetoxychavicol acetate 532379-01-4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(synergistic suppression of superoxide and **nitric oxide** generation from inflammatory cells by combined **food** factors)
REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 11 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:5914 HCAPLUS
DOCUMENT NUMBER: 138:66698
TITLE: Nitro-oxy compounds for the treatment of chronic pain
INVENTOR(S): Del Soldato, Piero; Ongini, Ennio
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2003000642	A2	20030103	WO 2002-EP5166
			2002
			0510
			<--
WO 2003000642	A3	20030327	
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, OM, PH, PL, RO, SG, SI, SK, TN, TR, TT, UA, US, UZ, VN, YU, ZA			
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2450538	AA	20030103	CA 2002-2450538
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EP 1417165	A2	20040512	EP 2002-742986
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
US 2004171682	A1	20040902	US 2003-480805
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PRIORITY APPLN. INFO.:			IT 2001-MI1308 A
			2001
			0621
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			WO 2002-EP5166 W
			2002
			0510
			<--

OTHER SOURCE(S): MARPAT 138:66698

AB Nitro-oxy derivative compds. or salts thereof having the general formula A(B)b0(C)c0NO2 (b0, c0 = 0, 1; A = RT1; R = radical of analgesic drug for chronic pain, in particular for neuropathic pain; B is such that its precursor is selected from amino acids, hydroxyacids, polyalcs., compds. containing at least one acid function; C is a bivalent radical containing an aliphatic, heterocyclic or aromatic radical). Preparation of selected compds., e.g. 1-(aminomethyl)cyclohexaneacetic acid 3-(nitrooxymethyl)phenyl hydrochloride ester, is described.

IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study) (donors; nitro-oxy compds. for treatment of chronic pain, and use with other agents)

RN 10102-43-9 HCAPLUS

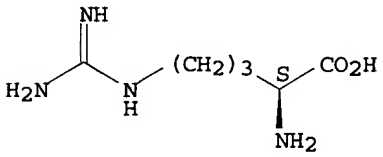
CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

N═O

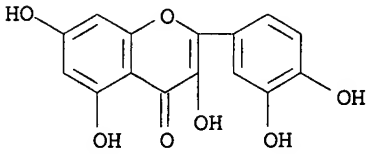
IT **74-79-3D**, Arginine, derivs. **117-39-5D**, Quercetin, derivs. **154-23-4D**, Catechin, derivs.
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(nitro-oxy compds. for treatment of chronic pain, and use with other agents)

RN 74-79-3 HCAPLUS
CN L-Arginine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

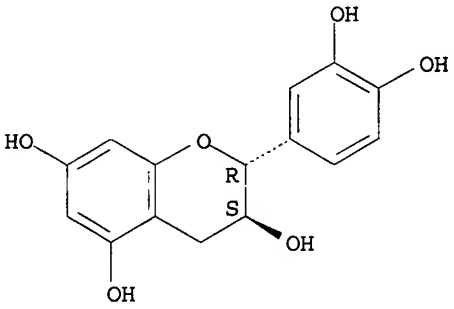


RN 117-39-5 HCAPLUS
CN 4H-1-Benzopyran-4-one, 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy- (9CI) (CA INDEX NAME)



RN 154-23-4 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IC ICM C07C203-04
ICS A61K031-21
CC 1-11 (Pharmacology)
Section cross-reference(s): 25
IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(donors; nitro-oxy compds. for treatment of chronic pain, and use with other agents)
IT 50-47-5, Desipramine 50-47-5D, Desipramine, derivs. 50-48-6, Amitriptyline 50-49-7, Imipramine 50-81-7D, Ascorbic acid, derivs. 52-67-5D, Penicillamine, derivs. 52-90-4D, Cysteine, derivs. 57-50-1D, Saccharose, derivs. 59-92-7D, Dopa, derivs. 60-00-4D, Edetic acid, derivs. 70-18-8D, Glutathione, derivs. 72-69-5, Nortriptyline 72-69-5D, Nortriptyline, derivs. **74-79-3D**, Arginine, derivs. 77-92-9D, Citric acid, derivs. 80-72-8D, Reductic acid, derivs. 89-65-6D, Isoascorbic acid, derivs. 110-17-8D, Fumaric acid, derivs. 111-17-1D, 3,3'-Thiodipropionic acid, derivs. 113-53-1, Dothiepin **117-39-5D**, Quercetin, derivs. 120-05-8D, Sulfuretin,

derivs. 121-34-6D, Vanillic acid, derivs. 121-79-9D, Propyl gallate, derivs. 123-31-9D, Hydroquinone, derivs. 149-91-7D, Gallic acid, derivs. **154-23-4D**, Catechin, derivs. 298-46-4, Carbamazepine 298-46-4D, Carbamazepine, derivs. 303-45-7D, Gossypol, derivs. 303-49-1, Clomipramine 305-84-0D, L-Carnosine, derivs. 306-60-5D, Agmatine, derivs. 315-30-0D, Allopurinol, derivs. 315-72-0, , Opipramol 315-72-0D, Opipramol, derivs. 331-39-5D, Caffeic acid, derivs. 438-60-8, Protriptyline 458-35-5D, Coniferyl alcohol, derivs. 490-79-9D, Gentisic acid, derivs. 500-38-9D, Nordihydroguaiaretic acid, derivs. 501-94-0D, derivs. 520-18-3D, Kaempferol, derivs. 526-84-1D, Dihydroxymaleic acid, derivs. 533-73-3D, Hydroxyhydroquinone, derivs. 584-85-0D, Anserine, derivs. 616-91-1D, N-Acetylcysteine, derivs. 739-71-9, Trimipramine 824-46-4D, Methoxyhydroquinone, derivs. 1078-61-1D, Dihydrocaffeic acid, derivs. 1135-24-6D, Ferulic acid, derivs. 1464-42-2D, Selenomethionine, derivs. 1668-19-5, Doxepin 3362-45-6, Noxiptilin 3614-08-2D, Selenocysteine, derivs. 3690-05-9D, p-Cumaric alcohol, derivs. 4498-32-2, Dibenzepin 4757-55-5, Dimetacrine 5118-29-6, Melitracen 5560-72-5, Iprindole 6600-40-4D, Norvaline, derivs. 7400-08-0D, p-Cumaric acid, derivs. 10321-12-7, Propizepine 14028-44-5, Amoxapine 14028-44-5D, Amoxapine, derivs. 15537-71-0D, N-Acetylpenicillamine, derivs. 23047-25-8, Lofepramine 24701-51-7, , Demexiptiline 24701-51-7D, Demexiptiline, derivs. 25451-15-4, Felbamate 25451-15-4D, Felbamate, derivs. 30223-48-4, Fluacizine 35941-65-2, Butriptyline 57574-09-1, Amineptine 57574-09-1D, Amineptine, derivs. 60142-96-3D, Gabapentin, derivs. 63147-28-4D, 3,5-Di-tert-butyl-4-hydroxybenzylthio glycolate, derivs. 68291-97-4, Zonisamide 68291-97-4D, Zonisamide, derivs. 68506-86-5D, Vigabatrin, derivs. 72797-41-2, Tianeptine 72797-41-2D, Tianeptine, derivs. 84057-84-1, Lamotrigine 84057-84-1D, Lamotrigine, derivs. 92614-59-0D, Glutathione ethyl ester, derivs. 97240-79-4, Topiramate 97240-79-4D, Topiramate, derivs. 97451-46-2D, Glutathione isopropyl ester, derivs. 115103-54-3, Tiagabine 115103-54-3D, Tiagabine, derivs. 148553-50-8D, Pregabalin, derivs. 156719-37-8D, derivs. 175033-36-0
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479674-15-2 479674-17-4 479674-19-6 479674-21-0
RL: PAC (Pharmacological activity); **THU (Therapeutic use)** ; BIOL (Biological study); USES (Uses)
(nitro-oxy compds. for treatment of chronic pain, and use with other agents)

L41 ANSWER 12 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:737552 HCAPLUS
DOCUMENT NUMBER: 138:297305
TITLE: Protective effects of the flavonoid quercetin in chronic **nitric oxide** deficient rats
AUTHOR(S): Duarte, Juan; Jimenez, Rosario; O'Valle, Francisco; Galisteo, Milagros; Perez-Palencia, Raquel; Vargas, Felix; Perez-Vizcaino, Francisco; Zarzuelo, Antonio; Tamargo, Juan
CORPORATE SOURCE: Department of Pharmacology, School of Medicine, University of Granada, Granada, Spain
SOURCE: Journal of Hypertension (2002), 20(9), 1843-1854
CODEN: JOHYD3; ISSN: 0263-6352

PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present study analyzed, for the first time, the effects of the flavonoid quercetin in rats after chronic inhibition of **nitric oxide** (NO) synthesis with -nitro-> **l-arginine** Me ester (>l-NAME). Rats were divided randomly into five different treatment groups for 6 wk: (1) vehicle (control, 1 mL of 1% methylcellulose once daily); (2) vehicle plus >l-NAME (75 mg/100 mL in drinking water); (3) quercetin (10 mg/kg p.o. once daily); (4) quercetin (5 mg/kg p.o.) plus >l-NAME; and (5) quercetin (10 mg/kg p.o.) plus >l-NAME. The evolution of systolic blood pressure, morphol. variables, proteinuria, plasma malondialdehyde and nitrite and nitrate concns., hepatic glutathione and malondialdehyde content, glutathione enzymes activity and vascular reactivity at the end of the experiment were analyzed. Quercetin markedly inhibited the development of >l-NAME-induced hypertension. This effect was accompanied by a partial or full prevention of most of the effects induced by >l-NAME, such as: (1) increases in the left ventricular and kidney weight indexes; (2) proteinuria; (3) renal histol. lesions, including hyaline arteriopathy and thickening of the vascular wall with moderate decrease of the lumen; (4) increased endothelium-dependent contraction; (5) increased vascular thromboxane B2 (TXB2) synthesis; (6) reduced plasma concns. of nitrites plus nitrates (NOx); (7) increased plasma and hepatic malondialdehyde (MDA) concns.; and (8) reduced glutathione peroxidase activity. In most cases these effects were dose dependent, but none of them were observed in normotensive animals. CONCLUSIONS This study confirms and extends the previous evidence about the antihypertensive effects and end-organ protection of the flavonoid quercetin in animal models of hypertension.

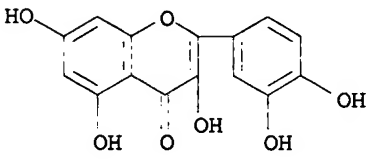
IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(protective effects of flavonoid quercetin in chronic **nitric oxide** deficient rats)

RN 10102-43-9 HCAPLUS
CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

N═O

IT **117-39-5**, Quercetin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protective effects of flavonoid quercetin in chronic **nitric oxide** deficient rats)

RN 117-39-5 HCAPLUS
CN 4H-1-Benzopyran-4-one, 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy- (9CI) (CA INDEX NAME)



CC 1-8 (Pharmacology)
ST cytoprotective flavonoid quercetin **nitric oxide** hypertension
IT Blood vessel, disease

(endothelium; protective effects of flavonoid quercetin in chronic **nitric oxide** deficient rats)

IT Antihypertensives
Cytoprotective agents
Heart
Kidney
Lipid peroxidation
Vasoconstriction
(protective effects of flavonoid quercetin in chronic **nitric oxide** deficient rats)

IT Lipid peroxidation
Reactive oxygen species
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(protective effects of flavonoid quercetin in chronic **nitric oxide** deficient rats)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proteinuria; protective effects of flavonoid quercetin in chronic **nitric oxide** deficient rats)

IT Endothelium
(vascular, disease; protective effects of flavonoid quercetin in chronic **nitric oxide** deficient rats)

IT 70-18-8, Glutathione, biological studies 7782-44-7D, Oxygen, reactive species 9001-48-3, Glutathione reductase 9013-66-5, Glutathione peroxidase **10102-43-9, Nitric oxide**, biological studies 54397-85-2, Thromboxane B2 329900-75-6, Cyclooxygenase 2 329967-85-3, Cyclooxygenase 1 501433-35-8, Inducible **nitric oxide synthase** 503473-02-7, Endothelial **nitric oxide synthase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(protective effects of flavonoid quercetin in chronic **nitric oxide** deficient rats)

IT **117-39-5**, Quercetin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protective effects of flavonoid quercetin in chronic **nitric oxide** deficient rats)

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 13 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:495905 HCAPLUS
DOCUMENT NUMBER: 138:117263
TITLE: In vitro and in vivo inhibitory activities of rutin, wogonin, and quercetin on **lipopolysaccharide**-induced **nitric oxide** and prostaglandin E2 production
AUTHOR(S): Shen, Shing-Chuan; Lee, Woan-Ruoh; Lin, Hui-Yi; Huang, Ho-Chun; Ko, Ching-Huai; Yang, Ling-Ling; Chen, Yen-Chou
CORPORATE SOURCE: Department of Dermatology, Taipei Medical University, School of Medicine, Taipei, Taiwan
SOURCE: European Journal of Pharmacology (**2002**), 446(1-3), 187-194
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

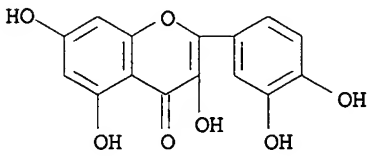
AB Flavonoids are widely distributed in plants, but their biol. functions are still unclear. In the present study, in vitro and in vivo expts. were performed to demonstrate the inhibitory activities of rutin, wogonin, and quercetin on **lipopolysaccharide**-induced **nitric oxide**

(NO) and prostaglandin E2 production in RAW 264.7 macrophages, primary peritoneal macrophages, and Balb/c mice, resp. In vitro results showed that wogonin and quercetin dose-dependently suppressed **lipopolysaccharide**-induced NO production in RAW 264.7 macrophages and primary peritoneal macrophages without a notable cytotoxic effect on either cell types associated with a decrease in inducible **nitric oxide synthase** (iNOS) protein expression in both cells. Rutin, at 80 μM only, had a slight but obvious inhibitory effect on **lipopolysaccharide**-induced NO production in primary peritoneal macrophages. Both wogonin and quercetin attenuated **lipopolysaccharide**-induced prostaglandin E2 production in vitro. I.v. injection of **lipopolysaccharide** (10 mg/kg, i.v.) resulted in a time-dependent induction of NO production in serum, and pretreatment with the **l-arginine** analog N-nitro-**l-arginine** Me ester (l-NAME) blocked this induction. I.v. pretreatment of Balb/c mice with rutin, wogonin or quercetin for 1 h followed by **lipopolysaccharide** treatment significantly inhibited **lipopolysaccharide**-induced NO production, but no inhibition of prostaglandin E2 production was found. A decrease in iNOS protein, but not cyclooxygenase-2 protein, was detected in liver and lung specimens of **lipopolysaccharide**-treated Balb/c mice in the presence of rutin, wogonin or quercetin. In conclusion, data obtained both in vitro and in vivo suggest that wogonin and quercetin exert inhibitory activity on **lipopolysaccharide** -induced NO production through suppression of iNOS expression.

IT **125978-95-2, Nitric oxide synthase**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inducible; inhibitory activities of rutin, wogonin, and quercetin on **lipopolysaccharide**-induced **nitric oxide** and PGE2 production)
RN 125978-95-2 HCAPLUS
CN Synthase, nitric oxide (9CI) (CA INDEX NAME)

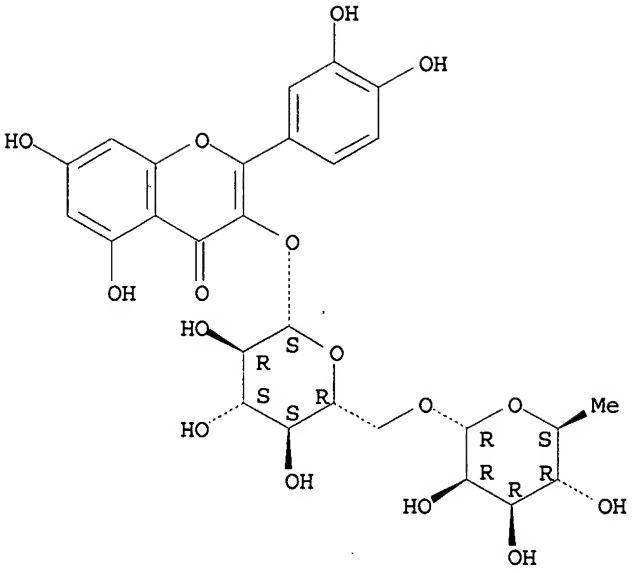
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **117-39-5**, Quercetin **153-18-4**, Rutin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitory activities of rutin, wogonin, and quercetin on **lipopolysaccharide**-induced **nitric oxide** and PGE2 production)
RN 117-39-5 HCAPLUS
CN 4H-1-Benzopyran-4-one, 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy- (9CI) (CA INDEX NAME)



RN 153-18-4 HCAPLUS
CN 4H-1-Benzopyran-4-one, 3-[[6-O-(6-deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy]-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



CC 1-5 (Pharmacology)
ST flavonoid **lipopolysaccharide nitric oxide** PGE2
IT **Lipopolysaccharides**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(inhibitory activities of rutin, wogonin, and quercetin on **lipopolysaccharide**-induced **nitric oxide** and PGE2 production)
IT **125978-95-2, Nitric oxide synthase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inducible; inhibitory activities of rutin, wogonin, and quercetin on **lipopolysaccharide**-induced **nitric oxide** and PGE2 production)
IT 363-24-6, Prostaglandin E2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitory activities of rutin, wogonin, and quercetin on **lipopolysaccharide**-induced **nitric oxide** and PGE2 production)
IT **117-39-5**, Quercetin **153-18-4**, Rutin 632-85-9, Wogonin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitory activities of rutin, wogonin, and quercetin on **lipopolysaccharide**-induced **nitric oxide** and PGE2 production)
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:203998 HCAPLUS
DOCUMENT NUMBER: 137:41520
TITLE: Mechanisms of relaxant action of 3-O-methylquercetin in isolated guinea pig trachea
AUTHOR(S): Ko, Wun-Chang; Wang, Han-Lang; Lei, Chien-Bang; Shih, Chih-Hsien; Chung, Mei-Ing; Lin, Chung-Nan
CORPORATE SOURCE: Graduate Institute of Medical Sciences, Taipei

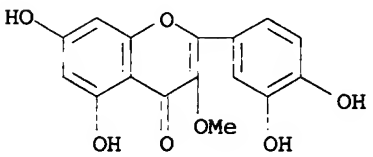
Medical University, Taipei, 110, Taiwan
SOURCE: Planta Medica (2002), 68(1), 30-35
CODEN: PLMEAA; ISSN: 0032-0943
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We investigated the mechanisms of action of 3-O-methylquercetin (3-MQ), isolated from Rhamnus nakaharai (Hayata) Hayata (Rhamnaceae) which is used as a folk medicine for treating constipation, inflammation, tumors and asthma in Taiwan. The tension changes of tracheal segments were isometrically recorded on a polygraph. 3-MQ concentration-dependently relaxed histamine (30 μM)-, carbachol (0.2 μM)- and KCl (30 mM)-induced precontractions, and inhibited cumulative histamine-, and carbachol-induced contractions in a non-competitive manner, 3-MQ also concentration-dependently and non-competitively inhibited cumulative Ca2+-induced contractions in depolarized (K+, 60 mM) guinea-pig trachealis. The nifedipine (10 μM)-remaining tension of histamine (30 μM)-induced precontraction was further relaxed by 3-MQ, suggesting that no matter whether VDCCs were blocked or not, 3-MQ may have other mechanisms of relaxant action. The relaxant effect of 3-MQ was unaffected by the removal of epithelium or by the presence of propranolol (1 μM), 2',5'-dideoxyadenosine (10 μM), methylene blue (25 μM), glibenclamide (10 μM), Nω-nitro- **L-arginine** (20 μM), or α-chymotrypsin (1 U/mL). However, 3-MQ (7.5-15 μM) and IBMX (3-6 μM), a pos. control, produced parallel and leftward shifts of the concentration-response curve of forskoline (0.01-3 μM) or nitroprusside (0.01-30 μM). 3-MQ or IBMX at various concns. (10-300 μM) concentration-dependently and significantly inhibited cAMP- and cGMP-PDE activities of the trachealis. The IC50 values of 3-MQ were estimated to be 13.8 and 14.3 μM, resp. The inhibitory effects of 3-MQ on both enzyme activities were not significantly different from those of IBMX, a non-selective PDE inhibitor. The above results reveal that the mechanisms of relaxant action of 3-MQ may be due to its inhibitory effects on both PDE activities and its subsequent reducing effect on [Ca2+]i of the trachealis.

IT **125978-95-2, Nitric oxide synthase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mechanisms of relaxant action of 3-O-methylquercetin in isolated guinea pig trachea)
RN 125978-95-2 HCAPLUS
CN Synthase, nitric oxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **1486-70-0**, 3-O-Methylquercetin
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanisms of relaxant action of 3-O-methylquercetin in isolated guinea pig trachea)
RN 1486-70-0 HCAPLUS
CN 4H-1-Benzopyran-4-one, 2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-3-methoxy- (9CI) (CA INDEX NAME)



CC 1-9 (Pharmacology)
IT 60-92-4, CAMP 7665-99-8, CGMP 9012-42-4, Adenylate cyclase
9036-21-9, CAMP-Phosphodiesterase 9054-75-5, Guanylate cyclase
9068-52-4, CGMP-Phosphodiesterase **125978-95-2**,
Nitric oxide synthase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mechanisms of relaxant action of 3-O-methylquercetin in isolated guinea pig trachea)
IT **1486-70-0**, 3-O-Methylquercetin
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanisms of relaxant action of 3-O-methylquercetin in isolated guinea pig trachea)
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 15 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:780607 HCAPLUS
DOCUMENT NUMBER: 135:327343
TITLE: **Polyphenol**-containing compositions and methods for improving vascular health
INVENTOR(S): Schmitz, Harold H.; Chevaux, Kati A.; Dombroski, Amy; Jerome, Ralph
PATENT ASSIGNEE(S): Mars, Inc., USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001078529	A2	20011025	WO 2001-US11542	2001 0410
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WO 2001078529	A3	20020321		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
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CA 2405731	AA	20011025	CA 2001-2405731	2001 0410
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US 2002018807	A1	20020214	US 2001-829782	2001 0410
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US 6610320	B2	20030826		
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EP 1274319	A2	20030115	EP 2001-926782	2001

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JP 2003530410 T2 20031014 JP 2001-575840
2001
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IL 152175 A1 20050831 IL 2001-152175
2001
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ZA 2002008130 A 20040122 ZA 2002-8130
2002
1009
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US 2004081715 A1 20040429 US 2003-458546
2003
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PRIORITY APPLN. INFO.: US 2000-197135P P
2000
0414
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US 2001-829782 A3
2001
0410
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WO 2001-US11542 W
2001
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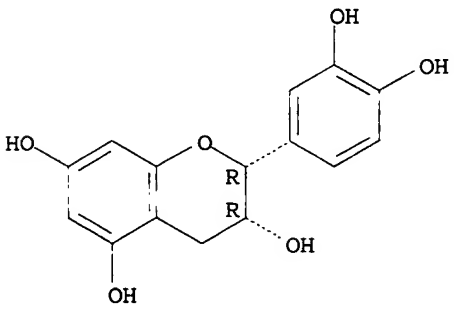
AB The invention provides compns. containing **polyphenols**, e.g. **cocoa polyphenols** such as procyanidins, in combination with at least one cholesterol-lowering agent, as well as methods for improving vascular health, including treating and preventing atherosclerosis and cardiovascular disease.

IT **490-46-0**, (-)-Epicatechin
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**polyphenol**-containing compns. and methods for improving vascular health)

RN 490-46-0 HCAPLUS

CN 2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-, (2R,3R)- (9CI) (CA INDEX NAME)

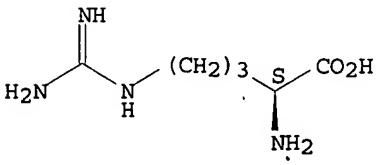
Absolute stereochemistry. Rotation (-).



IT **74-79-3**, **L-Arginine**, biological studies **154-23-4**, (+)-Catechin

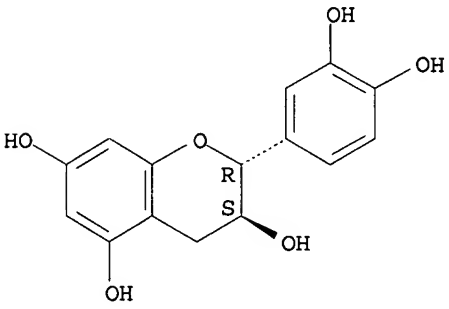
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**polyphenol**-containing compns. and methods for improving vascular health)
RN 74-79-3 HCAPLUS
CN L-Arginine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 154-23-4 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **10102-43-9, Nitric oxide**, biological studies **125978-95-2, Nitric oxide synthase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**polyphenol**-containing compns. and methods for improving vascular health)
RN 10102-43-9 HCAPLUS
CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

RN 125978-95-2 HCAPLUS
CN Synthase, nitric oxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IC ICM A23L001-30
ICS A23G001-00; A23G003-00; A23L001-305; A61K035-00
CC 1-8 (Pharmacology)
Section cross-reference(s): 18, 63
ST cardiovascular agent **cocoa polyphenol** procyanadin hypocholesterolemic
IT Selectins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(P-; **polyphenol**-containing compns. and methods for

improving vascular health)
IT Monocyte
(adhesion; **polyphenol**-containing compns. and methods for improving vascular health)
IT **Cocoa** products
(beverages; **polyphenol**-containing compns. and methods for improving vascular health)
IT Candy
(**chocolate**-covered; **polyphenol**-containing compns. and methods for improving vascular health)
IT DNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(damage; **polyphenol**-containing compns. and methods for improving vascular health)
IT Confectionery
(dark **chocolate**, phytosterol-containing; **polyphenol**-containing compns. and methods for improving vascular health)
IT **Chocolate**
(dark, phytosterol-containing; **polyphenol**-containing compns. and methods for improving vascular health)
IT Blood vessel
(endothelium; **polyphenol**-containing compns. and methods for improving vascular health)
IT Lipoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(low-d.; **polyphenol**-containing compns. and methods for improving vascular health)
IT Cell adhesion
(monocyte; **polyphenol**-containing compns. and methods for improving vascular health)
IT Fatty acids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monounsatd.; **polyphenol**-containing compns. and methods for improving vascular health)
IT Pet animal
(pet **food**; **polyphenol**-containing compns. and methods for improving vascular health)
IT Antioxidants
(pharmaceutical; **polyphenol**-containing compns. and methods for improving vascular health)
IT Confectionery
(phytosterol-containing toffee chews; **polyphenol**-containing compns. and methods for improving vascular health)
IT Anticholesteremic agents
Anticoagulants
Antihypertensives
Bakery products
Beverages
Cardiovascular agents
Chocolate
Cocoa products
Confectionery
Drug delivery systems
Food
Food additives
Oxidative stress, biological
Platelet (blood)
Platelet aggregation inhibitors
Vasodilators
(**polyphenol**-containing compns. and methods for improving vascular health)

IT Carotenes, biological studies
Flavanols
Procyanidins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**polyphenol**-containing compns. and methods for improving vascular health)

IT Phenols, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**polyphenols**, nonpolymeric; **polyphenol**-containing compns. and methods for improving vascular health)

IT Fatty acids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyunsatd.; **polyphenol**-containing compns. and methods for improving vascular health)

IT Proliferation inhibition
(proliferation inhibitors; **polyphenol**-containing compns. and methods for improving vascular health)

IT Blood vessel
(smooth muscle; **polyphenol**-containing compns. and methods for improving vascular health)

IT **Food**
(snack, granola bar; **polyphenol**-containing compns. and methods for improving vascular health)

IT Dietary fiber
(soluble; **polyphenol**-containing compns. and methods for improving vascular health)

IT Proteins, general, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(soybean; **polyphenol**-containing compns. and methods for improving vascular health)

IT Sterols
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(stanols, sterol- or stanol-based cholesterol-lowering agent; **polyphenol**-containing compns. and methods for improving vascular health)

IT Sterols
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sterol- or stanol-based cholesterol-lowering agent; **polyphenol**-containing compns. and methods for improving vascular health)

IT Diet
(supplements; **polyphenol**-containing compns. and methods for improving vascular health)

IT Biological transport
(uptake, **polyphenol**; **polyphenol**-containing compns. and methods for improving vascular health)

IT Drugs
(veterinary; **polyphenol**-containing compns. and methods for improving vascular health)

IT Integrins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(αIIbβ3; **polyphenol**-containing compns. and methods for improving vascular health)

IT 57-88-5, Cholesterol, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(**polyphenol**-containing compns. and methods for improving vascular health)

IT **490-46-0**, (-)-Epicatechin
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**polyphenol**-containing compns. and methods for improving vascular health)

IT 50-81-7, Vitamin C, biological studies **74-79-3**, **L-Arginine**, biological studies **154-23-4**, (+)-Catechin 1406-18-4, Vitamin E 7439-95-4, Magnesium, biological studies 7440-09-7, Potassium, biological studies 7440-70-2, Calcium, biological studies 9000-30-0, Guar gum 12001-76-2, Vitamin B
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**polyphenol**-containing compns. and methods for improving vascular health)

IT 363-24-6, PGE2 9029-60-1, Lipoxygenase **10102-43-9**, **Nitric oxide**, biological studies 39391-18-9, Cyclooxygenase 54397-85-2, TXB2 58962-34-8 116243-73-3, Endothelin **125978-95-2**, **Nitric oxide synthase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**polyphenol**-containing compns. and methods for improving vascular health)

IT 91037-65-9
RL: PRP (Properties)
(unclaimed sequence; **polyphenol**-containing compns. and methods for improving vascular health)

L41 ANSWER 16 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:596841 HCAPLUS
DOCUMENT NUMBER: 135:366462
TITLE: Inhibition of **nitric oxide synthase** inhibitors and **lipopolysaccharide** induced inducible NOS and cyclooxygenase-2 gene expressions by rutin, quercetin, and quercetin pentaacetate in RAW 264.7 macrophages
AUTHOR(S): Chen, Yen-Chou; Shen, Shing-Chuan; Lee, Woan-Ruoh; Hou, Wen-Chi; Yang, Ling-Ling; Lee, Tony J. F.
CORPORATE SOURCE: Graduate Institute of Pharmacognosy Science, Taipei Medical University, Taipei, Taiwan
SOURCE: Journal of Cellular Biochemistry (**2001**), 82(4), 537-548
CODEN: JCEBD5; ISSN: 0730-2312
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several natural flavonoids have been demonstrated to perform some beneficial biol. activities, however, higher-effective concns. and poor-absorptive efficacy in body of flavonoids blocked their practical applications. In the present study, we provided evidences to demonstrate that flavonoids rutin, quercetin, and its acetylated product quercetin pentaacetate were able to be used with **nitric oxide synthase** (NOS) inhibitors (N-nitro-**L-arginine** (NLA) or N-nitro-**L-arginine** Me ester (L-NAME)) in treatment of **lipopolysaccharide** (LPS) induced **nitric oxide** (NO) and prostaglandin E2 (PGE2) productions, inducible **nitric oxide**

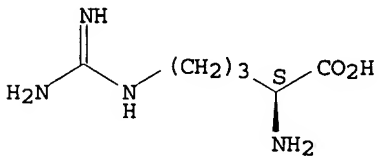
synthase (iNOS) and cyclooxygenase-2 (COX-2) gene expressions in a mouse macrophage cell line (RAW 264.7). The results showed that rutin, quercetin, and quercetin pentaacetate-inhibited LPS-induced NO production in a concentration-dependent manner without obvious cytotoxic effect on cells by MTT assay using 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazoliumbromide as an indicator. Decrease of NO production by flavonoids was consistent with the inhibition on LPS-induced iNOS gene expression by western blotting. However, these compds. were unable to block iNOS enzyme activity by direct and indirect measurement on iNOS enzyme activity. Quercetin pentaacetate showed the obvious inhibition on LPS-induced PGE2 production and COX-2 gene expression and the inhibition was not result of suppression on COX-2 enzyme activity. Previous study demonstrated that decrease of NO production by **L-arginine** analogs effectively stimulated LPS-induced iNOS gene expression, and proposed that stimulatory effects on iNOS protein by NOS inhibitors might be harmful in treating sepsis. In this study, NLA or L-NAME treatment stimulated significantly on LPS-induced iNOS (but not COX-2) protein in RAW 264.7 cells which was inhibited by these three compds. Quercetin pentaacetate, but not quercetin and rutin, showed the strong inhibitory activity on PGE2 production and COX-2 protein expression in NLA/LPS or L-NAME/LPS co-treated RAW 264.7 cells. These results indicated that combinatorial treatment of **L-arginine** analogs and flavonoid derivates, such as quercetin pentaacetate, effectively inhibited LPS-induced NO and PGE2 productions, at the same time, inhibited enhanced expressions of iNOS and COX-2 genes.

IT **74-79-3D**, **L-Arginine**, analogs, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of NO synthase inhibitors and **lipopolysaccharide** induced inducible NOS and COX-2 gene expressions by rutin, quercetin, and quercetin pentaacetate in macrophages)

RN 74-79-3 HCAPLUS

CN L-Arginine (9CI) (CA INDEX NAME)

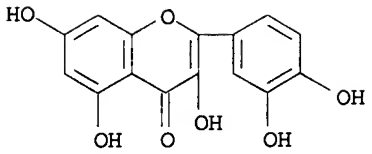
Absolute stereochemistry.



IT **117-39-5**, Quercetin **153-18-4**, Rutin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of NO synthase inhibitors and **lipopolysaccharide** induced inducible NOS and COX-2 gene expressions by rutin, quercetin, and quercetin pentaacetate in macrophages)

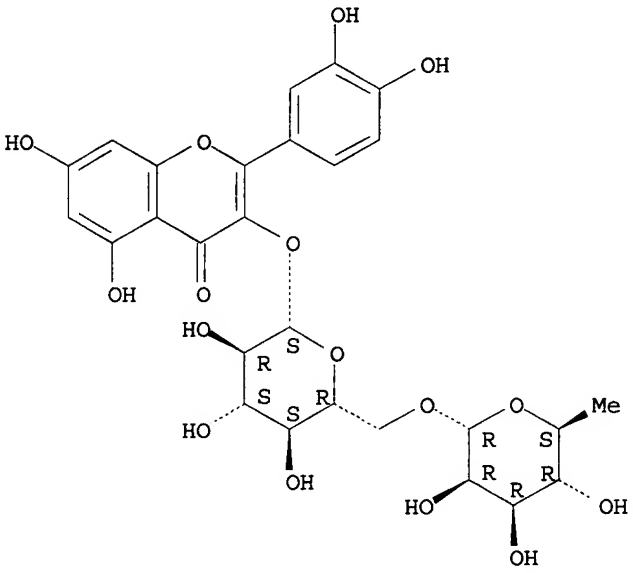
RN 117-39-5 HCAPLUS

CN 4H-1-Benzopyran-4-one, 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy- (9CI) (CA INDEX NAME)



RN 153-18-4 HCAPLUS
CN 4H-1-Benzopyran-4-one, 3-[[6-O-(6-deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy]-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 10102-43-9, **Nitric oxide**, biological studies **125978-95-2, Nitric oxide synthase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibition of NO synthase inhibitors and **lipopolysaccharide** induced inducible NOS and COX-2 gene expressions by rutin, quercetin, and quercetin pentaacetate in macrophages)
RN 10102-43-9 HCAPLUS
CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

RN 125978-95-2 HCAPLUS
CN Synthase, nitric oxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
CC 1-7 (Pharmacology)
Section cross-reference(s): 18
ST antiinflammatory flavonoid NO synthase COX2 gene macrophage; rutin quercetin pentaacetate **nitric oxide synthase** cyclooxygenase 2
IT Gene, animal

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(COX-2; inhibition of NO synthase inhibitors and **lipopolysaccharide** induced inducible NOS and COX-2 gene expressions by rutin, quercetin, and quercetin pentaacetate in macrophages)

IT Anti-inflammatory agents
Macrophage
(inhibition of NO synthase inhibitors and **lipopolysaccharide** induced inducible NOS and COX-2 gene expressions by rutin, quercetin, and quercetin pentaacetate in macrophages)

IT Flavonoids
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of NO synthase inhibitors and **lipopolysaccharide** induced inducible NOS and COX-2 gene expressions by rutin, quercetin, and quercetin pentaacetate in macrophages)

IT **74-79-3D**, **L-Arginine**, analogs, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of NO synthase inhibitors and **lipopolysaccharide** induced inducible NOS and COX-2 gene expressions by rutin, quercetin, and quercetin pentaacetate in macrophages)

IT 2149-70-4, Nitro-**L-arginine** 50903-99-6, L-NAME
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(inhibition of NO synthase inhibitors and **lipopolysaccharide** induced inducible NOS and COX-2 gene expressions by rutin, quercetin, and quercetin pentaacetate in macrophages)

IT **117-39-5**, Quercetin **153-18-4**, Rutin 1064-06-8, Quercetin pentaacetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of NO synthase inhibitors and **lipopolysaccharide** induced inducible NOS and COX-2 gene expressions by rutin, quercetin, and quercetin pentaacetate in macrophages)

IT 363-24-6, PGE2 **10102-43-9**, **Nitric oxide**, biological studies **125978-95-2**, **Nitric oxide synthase** 329900-75-6, Cyclooxygenase-2
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibition of NO synthase inhibitors and **lipopolysaccharide** induced inducible NOS and COX-2 gene expressions by rutin, quercetin, and quercetin pentaacetate in macrophages)

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 17 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:9198 HCAPLUS
DOCUMENT NUMBER: 134:188030
TITLE: Role of endothelium/**nitric oxide** in vascular response to flavonoids and epicatechin

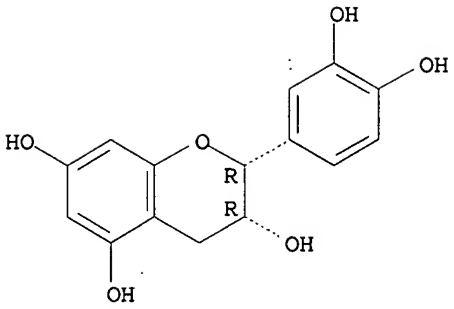
AUTHOR(S): Huang, Yu; Yao, Xiao-Qiang; Tsang, Suk Ying; Lau, Chi-Wai; Chen, Zhen-Yu
CORPORATE SOURCE: Departments of Physiology and Biochemistry, Faculty of Medicine, Chinese University of Hong Kong, Hong Kong, Peop. Rep. China
SOURCE: Acta Pharmacologica Sinica (2000), 21(12), 1119-1124
CODEN: APSCG5
PUBLISHER: Science Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB AIM: To examine the role of endothelium in the vascular responses to flavonoids, baicalein, baicalin, cardamonin, alpinetin, and to purified jasmine green tea (-)-epicatechin in the isolated rat mesenteric artery rings. METHODS: The isometric contraction was measured by Grass force-displacement transducers. RESULTS: Both baicalein and baicalin enhanced the phenylephrine-induced contractile response in the endothelium-intact rings. This enhancement was abolished by pretreatment with the **nitric oxide** inhibitor NG-nitro-**L-arginine** or in the absence of the endothelium. Both flavonoids also inhibited the acetylcholine-induced endothelial **nitric oxide**-dependent relaxation. In contrast, cardamonin, alpinetin or (-)-epicatechin induced both endothelium-dependent and -independent relaxation. NG-nitro-**L-arginine** meyhyl ester or endothelium denudation attenuated the endothelium-dependent relaxation to the same extent. CONCLUSION: Baicalein and baicalin enhanced the phenylephrine-induced contraction most likely through inhibiting production or/and release of endothelial **nitric oxide**. While, cardamonin-, alpinetin- or (-)epicatechin-induced endothelium-dependent relaxation is primarily mediated through endothelial **nitric oxide**.

IT **10102-43-9, Nitric oxide**, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(role of endothelium/**nitric oxide** in vascular response to flavonoids and epicatechin)
RN 10102-43-9 HCAPLUS
CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

N═O

IT **490-46-0**, (-)-Epicatechin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(role of endothelium/**nitric oxide** in vascular response to flavonoids and epicatechin)
RN 490-46-0 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



CC 1-8 (Pharmacology)
ST vascular endothelium **nitric oxide** flavonoid epicatechin
IT Blood vessel
(endothelium; role of endothelium/**nitric oxide** in vascular response to flavonoids and epicatechin)
IT Blood vessel
(role of endothelium/**nitric oxide** in vascular response to flavonoids and epicatechin)
IT Flavonoids
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(role of endothelium/**nitric oxide** in vascular response to flavonoids and epicatechin)
IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(role of endothelium/**nitric oxide** in vascular response to flavonoids and epicatechin)
IT **490-46-0**, (-)-Epicatechin 491-67-8, Baicalein 19309-14-9, Cardamonin 21967-41-9, Baicalin 36052-37-6, Alpinetin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(role of endothelium/**nitric oxide** in vascular response to flavonoids and epicatechin)
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 18 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:553409 HCAPLUS
DOCUMENT NUMBER: 133:159933
TITLE: **L-Arginine** based formulations for treating diseases and methods of using same
INVENTOR(S): Kaesemeyer, Wayne H.
PATENT ASSIGNEE(S): Nitrosystems, Inc., USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000045809 A1 20000810 WO 2000-US2798
2000
0204
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CA 2361575 AA 20000810 CA 2000-2361575
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EP 1150669 A1 20011107 EP 2000-911701
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
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PRIORITY APPLN. INFO.: US 1999-118903P P
1999
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EP 2000-911701 A3
2000
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WO 2000-US2798 W
2000
0204
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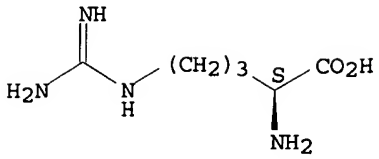
AB A therapeutic mixture comprised of **L-arginine** and a **nitric oxide synthase** agonist (e.g. doxazosin) is disclosed for the treatment of diseases, such as coronary heart disease and hypertension.

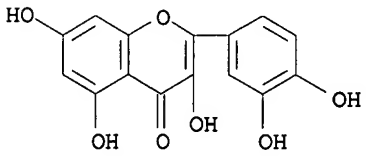
IT **74-79-3**, **L-Arginine**, biological studies **117-39-5**, Quercetin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)

RN 74-79-3 HCAPLUS
CN L-Arginine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 117-39-5 HCAPLUS
CN 4H-1-Benzopyran-4-one, 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy- (9CI) (CA INDEX NAME)



IT **10102-43-9, Nitric oxide**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
RN 10102-43-9 HCAPLUS
CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

IT **125978-95-2, Nitric oxide synthase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
RN 125978-95-2 HCAPLUS
CN Synthase, nitric oxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IC ICM A61K031-195
ICS A61K031-495; A61K035-78
CC 1-8 (Pharmacology)
Section cross-reference(s): 63
IT Artery
(angioplasty; therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
IT Drug delivery systems
(buccal; therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
IT Brain, disease
(cerebrovascular; therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
IT Artery, disease
(coronary, restenosis; therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
IT Artery, disease
(coronary; therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates

for vasodilation)
IT Cardiovascular system
(disease; therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
IT Elder (Sambucus)
Garlic (Allium sativum)
Ginkgo biloba
Hawthorn (Crataegus)
(exts.; therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
IT Heart, disease
(hypertensive; therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
IT Drug delivery systems
(inhalants; therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
IT Drug delivery systems
(injections, i.v.; therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
IT Drug delivery systems
(injections, s.c.; therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
IT Flavones
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(isoflavones, soy; therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
IT Drug delivery systems
(nasal; therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
IT Drug delivery systems
(oral; therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
IT Drug delivery systems
(parenterals; therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
IT Estrogens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phytoestrogens; therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
IT Drug delivery systems
(rectal; therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
IT Drug delivery systems
(sublingual; therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
IT Drug delivery systems
(tapes; therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
IT Hypercholesterolemia
Hypertension
Vasodilators
(therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)

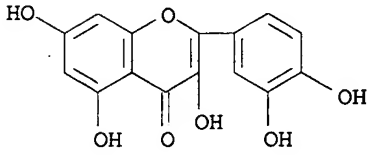
IT Drug delivery systems
(topical; therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
IT Adrenoceptor antagonists
(α1-; therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
IT 539-86-6, Allicin
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
IT 59-30-3, Folic acid, biological studies 73-31-4, Melatonin **74-79-3, L-Arginine**, biological studies 83-88-5, Riboflavin, biological studies **117-39-5**, Quercetin 501-36-0, Resveratrol 19216-56-9, Prazosin 63590-64-7, Terazosin 74191-85-8, Doxazosin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
IT **10102-43-9, Nitric oxide**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
IT **125978-95-2, Nitric oxide synthase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(therapeutic mixts. containing doxazosin and **nitric oxide synthase** substrates for vasodilation)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 19 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:64741 HCAPLUS
DOCUMENT NUMBER: 132:346968
TITLE: Endothelial NO release caused by red wine **polyphenols**
AUTHOR(S): Stoclet, J. C.; Kleschyov, A.; Andriambeloson, E.; Diebolt, M.; Andriantsitohaina, R.
CORPORATE SOURCE: Pharmacologie et Physico-chimie des Interactions Cellulaires et Moleculaires (UMR CNRS 7034), Universite Louis Pasteur de Strasbourg, ILLKIRCH, F-67401, Fr.
SOURCE: Journal of Physiology and Pharmacology (**1999**), 50(4), 535-540
CODEN: JPHPEI; ISSN: 0867-5910
PUBLISHER: Polish Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Epidemiol. studies have suggested that moderate consumption of red wine might reduce the risk of cardiovascular disease. Red Wine **Polyphenolic** Compds. (RWPC), a complex extract obtained from red wine, causes endothelium-dependent vasorelaxation in rat aortic rings pre-contracted with noradrenaline. This effect is associated with marked formation of NO in the vessel (directly shown by ESR spectroscopy) and it is abolished by the NO synthase inhibitor NG-nitro-**L-arginine** methylester (300 μM). It is mimicked by some defined **polyphenols**

(like the anthocyanin delphinidin) but not by others (malvidin, cyanidin, quercetin, catechin, epicatechin), despite close structures. In addition, RWPC causes an extracellular Ca2+-dependent increase in [Ca2+]i in endothelial but not in smooth muscle cells. The efficiency of RWPC in inducing NO production in the aorta and increase in [Ca2+]i, in endothelial cells is comparable to those of carbachol and bradykinin, resp. These findings provide evidence that RWPC and **polyphenols** with selective structures can activate an undefined target in endothelial cells. The resulting increase in [Ca2+]i activation of NO-synthase and enhanced formation of NO may be involved in cardiovascular protection.

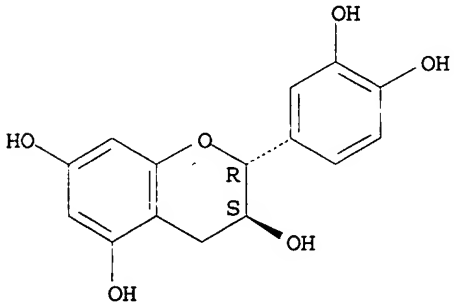
IT **117-39-5**, Quercetin **154-23-4**, Catechin
490-46-0, Epicatechin **528-58-5**, Cyanidin
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(endothelial **nitric oxide** release caused by red wine **polyphenols**)

RN 117-39-5 HCAPLUS
CN 4H-1-Benzopyran-4-one, 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy- (9CI) (CA INDEX NAME)



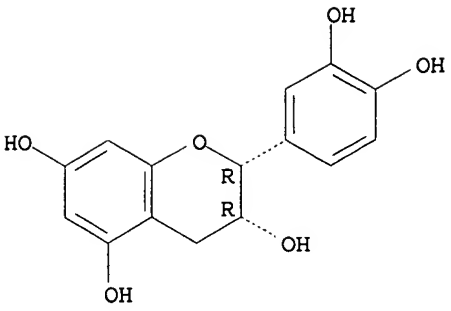
RN 154-23-4 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

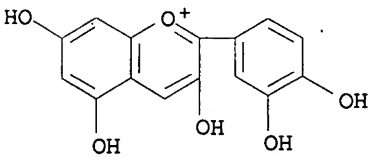


RN 490-46-0 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

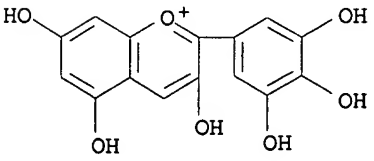


RN 528-58-5 HCAPLUS
CN 1-Benzopyrylium, 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-, chloride (9CI) (CA INDEX NAME)



● Cl⁻

IT **528-53-0**, Delphinidin
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(endothelial **nitric oxide** release caused by red wine **polyphenols**)
RN 528-53-0 HCAPLUS
CN 1-Benzopyrylium, 3,5,7-trihydroxy-2-(3,4,5-trihydroxyphenyl)-, chloride (9CI) (CA INDEX NAME)



● Cl⁻

IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(endothelial **nitric oxide** release caused by red wine **polyphenols**)
RN 10102-43-9 HCAPLUS
CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

N==O

CC 17-13 (Food and Feed Chemistry)
Section cross-reference(s): 1
ST red wine **polyphenol** endothelium **nitric oxide**
IT Biological transport
(calcium; endothelial **nitric oxide** release caused by red wine **polyphenols**)
IT Cytoprotective agents
(cardiovascular; endothelial **nitric oxide** release caused by red wine **polyphenols**)
IT Anthocyanins
Tannins
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(endothelial **nitric oxide** release caused by red wine **polyphenols**)
IT Vasodilators
(endothelium-dependent; endothelial **nitric oxide** release caused by red wine **polyphenols**)
IT Blood vessel
(endothelium; endothelial **nitric oxide** release caused by red wine **polyphenols**)
IT Phenols, biological studies
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(**polyphenols**, nonpolymeric; endothelial **nitric oxide** release caused by red wine **polyphenols**)
IT Wine
(red; endothelial **nitric oxide** release caused by red wine **polyphenols**)
IT **117-39-5**, Quercetin **154-23-4**, Catechin
490-46-0, Epicatechin **528-58-5**, Cyanidin
643-84-5, Malvidin
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(endothelial **nitric oxide** release caused by red wine **polyphenols**)
IT **528-53-0**, Delphinidin
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(endothelial **nitric oxide** release caused by red wine **polyphenols**)
IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(endothelial **nitric oxide** release caused by red wine **polyphenols**)
IT 7440-70-2, Calcium, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(transport; endothelial **nitric oxide** release caused by red wine **polyphenols**)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

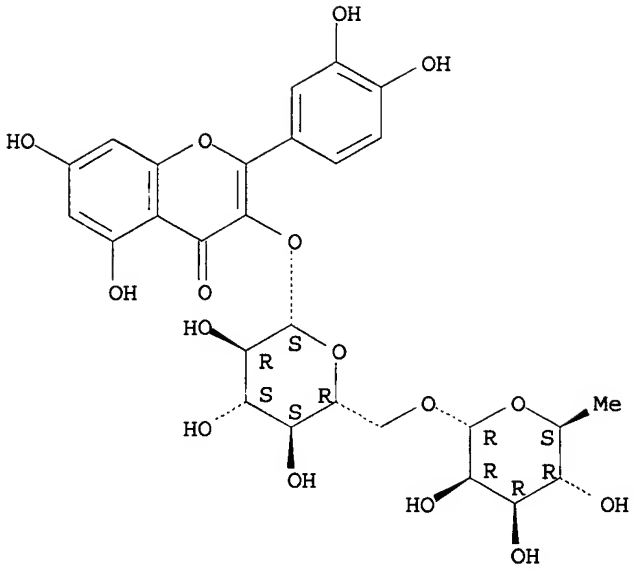
L41 ANSWER 20 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:729584 HCAPLUS
DOCUMENT NUMBER: 132:246145
TITLE: Protective effects of rutoside on gastric mucosa and influence on **nitric oxide** and prostaglandin
AUTHOR(S): Zhao, Weizhong; Cen, Deyi; Chen, Zhiwu; Wang, Yuling; Wang, Qiong; Li, Qianjin; Song, Biwei
CORPORATE SOURCE: Dept of Pharmacology, Anhui Medical University, Hefei, 230032, Peop. Rep. China
SOURCE: Zhongguo Yaolixue Tongbao (**1999**), 15(4), 360-362
CODEN: ZYTOE8; ISSN: 1001-1978
PUBLISHER: Anhui Yike Daxue Linchuan Yaoli Yanjiuso
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The relationship between the protective effect of rutoside on gastric mucosa and **nitric oxide** (NO) and prostaglandin (PG) was studied. The gastric mucosa of mice was injured by absolute ethanol; the lesion area of gastric mucosa was measured; the contents of NO and PGE2 of gastric tissue were determined; the effect of Ru on gastric mucosal injury induced by NG-nitro-**L-arginine** **L**-NNA + 30% ethanol was evaluated. The lesion area of gastric mucosa in mice was reduced dose-dependently after administration of Ru (7, 14, 28 mg kg-1, ig, bid x 5 d), and the inhibitory rates were 20.6%, 28.7% and 52.2%, resp. The decrease of NO content induced by ethanol was significantly elevated by Ru to normal level, but Ru did not influence the content of PGE2 in gastric tissue of mice. Ru (5, 20 mg kg-1, ig, bid x 5 d) could also significantly inhibit gastric mucosal injury in rats induced by NO synthase inhibitor L-NNA + 30% ethanol.

IT **153-18-4**, Rutoside
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protective effects of rutoside on gastric mucosa and effect on **nitric oxide** and prostaglandin)

RN 153-18-4 HCAPLUS
CN 4H-1-Benzopyran-4-one, 3-[[6-O-(6-deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy]-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(protective effects of rutoside on gastric mucosa and effect on **nitric oxide** and prostaglandin)
RN 10102-43-9 HCAPLUS
CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

N═O

CC 1-9 (Pharmacology)
IT Stomach
(mucosa; protective effects of rutoside on gastric mucosa and effect on **nitric oxide** and prostaglandin)
IT Cytoprotective agents
(protective effects of rutoside on gastric mucosa and effect on **nitric oxide** and prostaglandin)
IT **153-18-4**, Rutoside
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protective effects of rutoside on gastric mucosa and effect on **nitric oxide** and prostaglandin)
IT 363-24-6, Prostaglandin E2 **10102-43-9**, **Nitric oxide**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(protective effects of rutoside on gastric mucosa and effect on **nitric oxide** and prostaglandin)

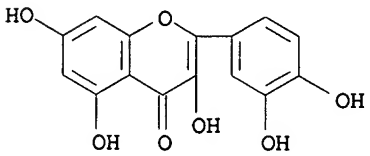
L41 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:544698 HCAPLUS
DOCUMENT NUMBER: 129:243100
TITLE: In vitro attenuation of **nitric oxide** production in C6 astrocyte cell culture by various dietary compounds
AUTHOR(S): Soliman, Karam F. A.; Mazzio, Elizabeth A.
CORPORATE SOURCE: College of Pharmacy and Pharmaceutical

Sciences, Florida A and M University, Tallahassee, FL, 32307, USA
SOURCE: Proceedings of the Society for Experimental Biology and Medicine (1998), 218(4), 390-397
CODEN: PSEBAA; ISSN: 0037-9727
PUBLISHER: Blackwell Science, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Excessive **nitric oxide** (NO) production in the brain has been correlated with neurotoxicity and pathogenesis of several neurodegenerative diseases. NO production from neuroglial cells surrounding neurons contributes to the pathogenesis of these diseases. The suppression of NO production in these cells may be beneficial in retarding many of these disorders. The ability of **polyphenolic** compds., flavonoids, crude exts., oils, and other **food** constituents to suppress the release of NO from **lipopolysaccharide** (LPS)/γ-interferon (IFN-γ) stimulated C6 astrocyte cells was studied in vitro. Of the 61 compds. tested, 36 showed significant suppressive effects of the NO production The following compds. had a dose-dependent suppressive effect of NO production with an IC50 <10-3 M: quercetin, (-)-epigallocatechin gallate, morin, curcumin, apigenin, sesamol, chlorogenic acid, fisetin, (+)-taxifolin, (+)-catechin, ellagic acid, and caffeic acid. Agents that decreased the NO production at concns. <300 ppm included milk thistle, silymarin, grapenol, and green tea. The results demonstrate a possible value for dietary compds. in the inhibition of excessive production of NO.

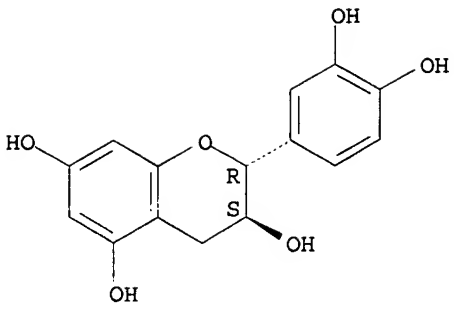
IT **117-39-5**, Quercetin **154-23-4**, + Catechin **480-18-2**, + Taxifolin **529-44-2**, Myricetin **989-51-5**, (-)-Epigallocatechin gallate **190836-14-7**, Rutin hydrate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**nitric oxide** production attenuation in C6 astrocyte cell culture by various dietary compds.)

RN 117-39-5 HCAPLUS
CN 4H-1-Benzopyran-4-one, 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy- (9CI) (CA INDEX NAME)



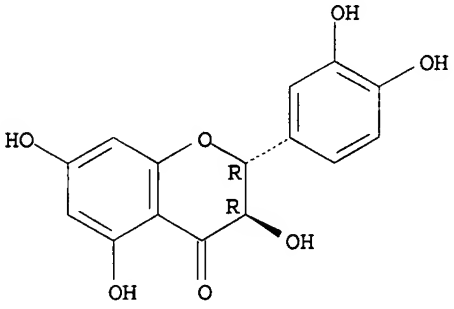
RN 154-23-4 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

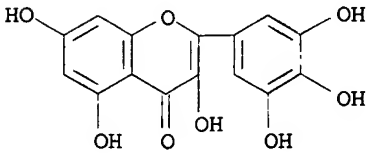


RN 480-18-2 HCAPLUS
CN 4H-1-Benzopyran-4-one, 2-(3,4-dihydroxyphenyl)-2,3-dihydro-3,5,7-trihydroxy-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

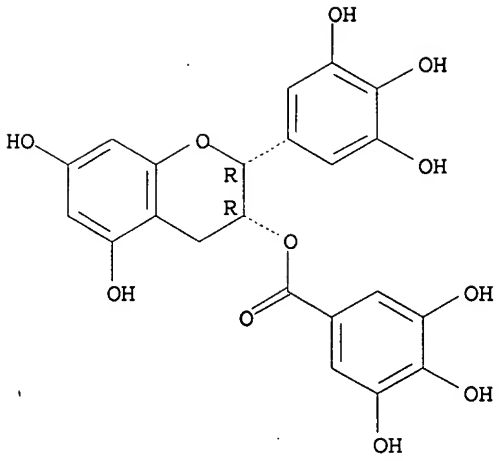


RN 529-44-2 HCAPLUS
CN 4H-1-Benzopyran-4-one, 3,5,7-trihydroxy-2-(3,4,5-trihydroxyphenyl)- (9CI) (CA INDEX NAME)



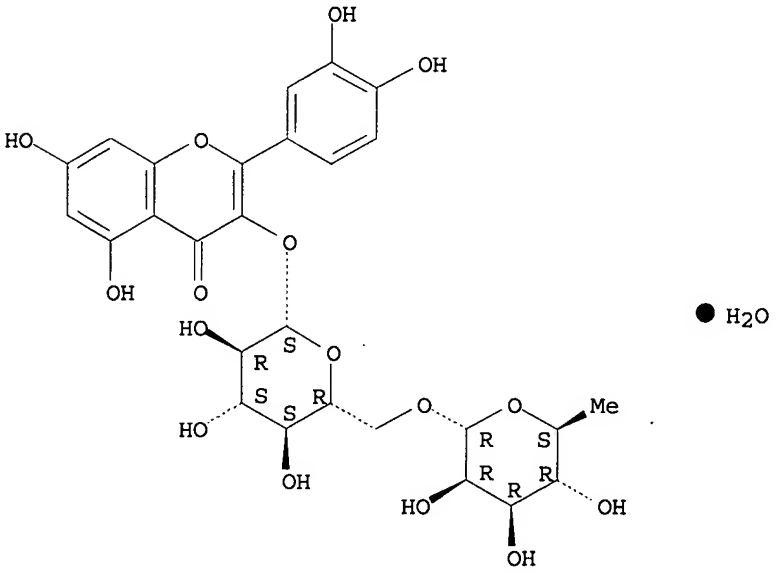
RN 989-51-5 HCAPLUS
CN Benzoic acid, 3,4,5-trihydroxy-, (2R,3R)-3,4-dihydro-5,7-dihydroxy-2-(3,4,5-trihydroxyphenyl)-2H-1-benzopyran-3-ylester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 190836-14-7 HCAPLUS
CN 4H-1-Benzopyran-4-one, 3-[[6-O-(6-deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy]-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-, monohydrate (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(**nitric oxide** production attenuation in C6 astrocyte cell culture by various dietary compds.)
RN 10102-43-9 HCAPLUS
CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

CC 13-6 (Mammalian Biochemistry)
Section cross-reference(s): 18
ST **nitric oxide** formation astrocyte **food** component
IT Tea products
(beverages, green; **nitric oxide** production attenuation in C6 astrocyte cell culture by various dietary compds.)
IT Essential oils
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(clove; **nitric oxide** production attenuation in C6 astrocyte cell culture by various dietary compds.)
IT Essential oils
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(garlic; **nitric oxide** production attenuation in C6 astrocyte cell culture by various dietary compds.)
IT Fats and Glyceridic oils, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(grape seed; **nitric oxide** production attenuation in C6 astrocyte cell culture by various dietary compds.)
IT Fats and Glyceridic oils, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(menhaden; **nitric oxide** production attenuation in C6 astrocyte cell culture by various dietary compds.)
IT Aloe barbadensis
Astrocyte
Food
Ginseng (Panax)
Propolis
Seaweed
(**nitric oxide** production attenuation in C6 astrocyte cell culture by various dietary compds.)
IT Canola oil
Cod liver oil
Linseed oil
Tocopherols
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**nitric oxide** production attenuation in C6 astrocyte cell culture by various dietary compds.)
IT Essential oils
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(rosemary; **nitric oxide** production attenuation in C6 astrocyte cell culture by various dietary compds.)
IT Cartilage
(shark; **nitric oxide** production attenuation in C6 astrocyte cell culture by various dietary compds.)
IT 50-02-2, Dexamethasone 53-86-1, Indomethacin 58-08-2, Caffeine, biological studies 58-32-2, Dipyridamole 73-31-4, Melatonin 77-52-1, Ursolic acid 89-83-8, Thymol 97-53-0, Eugenol 98-92-0, Niacin amide 107-35-7, Taurine 110-89-4, Piperidine, biological studies **117-39-5**, Quercetin **154-23-4**, + Catechin 275-51-4, Azulene 303-98-0, Coenzyme q10 315-30-0, Allopurinol 327-97-9, Chlorogenic acid 331-39-5, Caffeic acid 446-72-0, Genistein 458-37-7, Curcumin 476-66-4, Ellagic acid 480-16-0, Morin **480-18-2**, + Taxifolin 499-75-2, Carvacrol 520-26-3, Hesperidin 520-27-4, Diosmin 520-33-2, Hesperetin 520-36-5, Apigenin 528-48-3, Fisetin **529-44-2**, Myricetin 533-31-3, Sesamol 541-15-1, Carnitine 616-91-1, N-Acetyl cysteine **989-51-5**

, (-)-Epigallocatechin gallate 1135-24-6, Ferulic acid
2149-70-4, Nω-Nitro- **L-arginine**
2257-09-2, β Phenylethylisothiocyanate 5989-27-5, +
Limonene 6493-05-6, Pentoxifylline 10236-47-2, Naringin
14611-51-9, L-Deprenyl 65666-07-1, Silymarin **190836-14-7**
, Rutin hydrate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**nitric oxide** production attenuation in C6 astrocyte cell culture by various dietary compds.)

IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(**nitric oxide** production attenuation in C6 astrocyte cell culture by various dietary compds.)

REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 22 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:30749 HCAPLUS
DOCUMENT NUMBER: 128:127468
TITLE: Effect of red wine on endothelium-dependent relaxation in rabbits
AUTHOR(S): Cishek, Mary Beth; Galloway, Michael T.; Karim, Malina; German, J. Bruce; Kappagoda, C. Tissa
CORPORATE SOURCE: Division of Cardiovascular Medicine, University of California, Davis, CA, 95616, USA
SOURCE: Clinical Science (**1997**), 93(6), 507-511
CODEN: CSCIAE; ISSN: 0143-5221
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

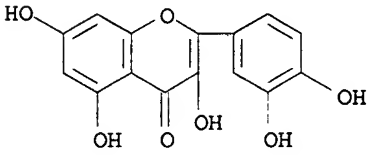
AB Published data on the effects of red wine, ethanol and flavonoids on endothelium-dependent relaxation are equivocal. The present study was under-taken to determine the effects of red wine, ethanol and selected flavonoids present in red wine on endothelium-dependent relaxation. Aortic rings from New Zealand White rabbits were set up in organ baths (20 mL) and contracted with noradrenaline (10-6 mol/l). An attempt was made to elicit dose-dependent relaxant responses to red wine (15, 30, 40, 80 or 120 μl), ethanol (5.4, 10.8 and 16.2 μl) and the flavonoids catechin, epicatechin, quercetin and polymeric phenols (10-7 to 10-4 mol/l). In some expts., endothelium-dependent relaxation to cumulative doses of acetylcholine (10-9 to 10-6 mol/l) was determined before and after incubating the rings for 15 min with red wine (120 μl), ethanol (16.2 μl), quercetin (10-5 mol/l), catechin (10-5 mol/l), epicatechin (10-5 mol/l) and PPs (10-5 mol/l) resp. CGMP was also measured in some rings in the control state and after addition of 120 μl of red wine, sodium nitroprusside (10-4 mol/l) and polymeric phenols (10-5 mol/l). 3. Red wine evoked a dose-dependent relaxation in aortic rings. The highest vols. of wine (120 μl) relaxed the vessels by 71.35 ± 7.89% of the maximal contraction (8.95 ± 0.97 g). Polymeric phenols also relaxed the precontracted rings. These responses were abolished by NG-**L-arginine** Me ester (L-NAME) and by removal of endothelium. Addition of red wine, polymeric phenols and sodium nitroprusside increased the cGMP content of the rings. In tissues previously incubated with red wine and polymeric phenols, endothelium-dependent relaxation in response to acetylcholine was attenuated. Ethanol had no such effect. Acute exposure of aortic

rings to red wine and polymeric phenols evokes an endothelium-dependent relaxation which is mediated by **nitric oxide**. However, prior exposure to both red wine and polymeric phenols has a second effect in that it attenuates the endothelium-dependent relaxation evoked by acetylcholine. Since this effect is restored by arginine, it is likely to be due to depletion of substrate for **nitric oxide synthase**.

IT **125978-95-2, Nitric oxide synthase**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(effect of red wine on endothelium-dependent relaxation in rabbits)
RN 125978-95-2 HCAPLUS
CN Synthase, nitric oxide (9CI) (CA INDEX NAME)

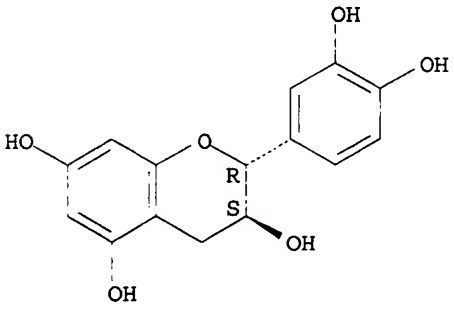
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **117-39-5**, Quercetin **154-23-4**, Catechin, biological studies **490-46-0**, Epicatechin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(effect of red wine on endothelium-dependent relaxation in rabbits)
RN 117-39-5 HCAPLUS
CN 4H-1-Benzopyran-4-one, 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy- (9CI) (CA INDEX NAME)



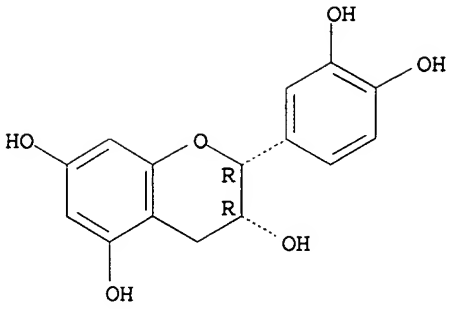
RN 154-23-4 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 490-46-0 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



CC 18-7 (Animal Nutrition)
Section cross-reference(s): 1
ST aorta relaxation red wine **polyphenol**; flavonoid wine aorta relaxation
IT **125978-95-2**, **Nitric oxide synthase**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(effect of red wine on endothelium-dependent relaxation in rabbits)
IT 64-17-5, Ethanol, biological studies **117-39-5**, Quercetin **154-23-4**, Catechin, biological studies **490-46-0**, Epicatechin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(effect of red wine on endothelium-dependent relaxation in rabbits)
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

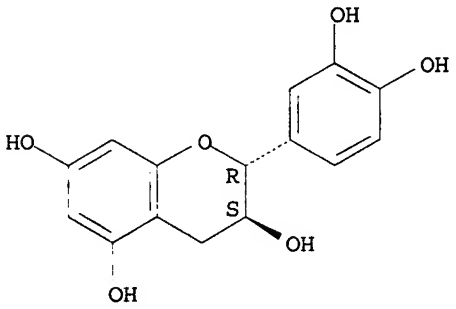
L41 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:212445 HCAPLUS
DOCUMENT NUMBER: 126:287787
TITLE: **Nitric oxide** production and endothelium-dependent vasorelaxation induced by wine **polyphenols** in rat aorta
AUTHOR(S): Andriambeloson, Emile; Kleschyov, Andrei L.; Muller, Bernard; Beretz, Alain; Stoclet, Jean Claude; Andriantsitohaina, Ramaroson
CORPORATE SOURCE: Laboratoire de Pharmacologie et Physiopathologie Cellulaires, Universite Louis Pasteur de Strasbourg, URA CNRS 600 Faculte de Pharmacie, Illkirch, 67401, Fr.
SOURCE: British Journal of Pharmacology (**1997**), 120(6), 1053-1058
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The aim of this work was to investigate the mechanism of vasorelaxation induced by red wine **polyphenolic** compds. (RWPC) and two defined **polyphenols** contained in wine, leucocyanidol and catechin. The role of the endothelium, especially endothelium-derived **nitric oxide** (NO), was also investigated. Relaxation produced by **polyphenols** was studied in rat aortic rings with and without functional endothelium, pre-contracted to the same extent with noradrenaline (0.3 and 0.1 μM, resp.). RWPC and leucocyanidol, but not

catechin, produced complete relaxation of vessels with and without endothelium. However, 1000 fold higher concns. were needed to relax endothelium-denuded rings compared to those with functional endothelium. High concns. of catechin (in the range of 10-1 g/I) only produced partial relaxation (maximum 30%) and had the same potency in rings with and without endothelium. The NO synthase inhibitor, Nω-nitro- **L-arginine** -methyl-ester (L-NAME, 300 μM) completely abolished the endothelium-dependent but not the endothelium-independent relaxations produced by all of the **polyphenolic** compds. In contrast to superoxide dismutase (SOD, 100 u/mL), neither RWPC nor leucocyanidol affected the concentration-response curve for the NO donor, SIN-1 (3-morpholino-sydnonimine) which also produces superoxide anion (O2-). In aortic rings with endothelium, RWPC (10-2 g/I) produced a 7 fold increase in the basal production of guanosine 3': 5'-cyclic monophosphate (cyclic GMP) which was prevented by L-NAME (300 μM). ESR (e.p.r.) spectroscopy studies with Fe2+-diethyldithiocarbamate as an NO spin trap demonstrated that RWPC and leucocyanidol increased NO levels in rat thoracic aorta about 2-fold. This NO production was entirely dependent on the presence of the endothelium and was abolished by L-NAME (300 μM). These results show that RWPC and leucocyanidol, but not the structurally closely related **polyphenol** catechin, induced endothelium-dependent relaxation in the rat aorta. They indicate that this effect results from enhanced synthesis of NO rather than enhanced biol. activity of NO or protection against breakdown by O2-. It is concluded that some **polyphenols**, with specific structure, contained in wine possess potent endothelium-dependent vasorelaxing activity.

IT **154-23-4**, Catechin **480-17-1**, Leucocyanidol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**nitric oxide** production and endothelium-dependent vasorelaxation induced by wine **polyphenols** in rat aorta)

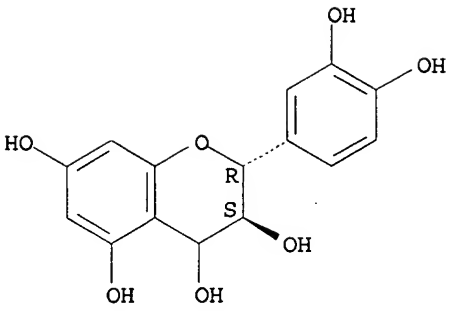
RN 154-23-4 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 480-17-1 HCAPLUS
CN 2H-1-Benzopyran-3,4,5,7-tetrol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

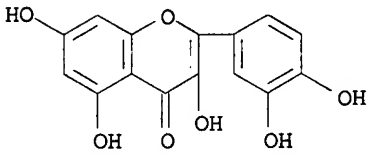


CC 1-8 (Pharmacology)
Section cross-reference(s): 18
ST vasorelaxation aorta wine **polyphenol**; catechin leucocyanidol wine aorta vasorelaxation
IT Artery
(aorta; **nitric oxide** production and endothelium-dependent vasorelaxation induced by wine **polyphenols** in rat aorta)
IT Blood vessel
(endothelium; **nitric oxide** production and endothelium-dependent vasorelaxation induced by wine **polyphenols** in rat aorta)
IT Vasodilation
Wine
(**nitric oxide** production and endothelium-dependent vasorelaxation induced by wine **polyphenols** in rat aorta)
IT Phenols, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**polyphenols**, nonpolymeric; **nitric oxide** production and endothelium-dependent vasorelaxation induced by wine **polyphenols** in rat aorta)
IT **154-23-4**, Catechin **480-17-1**, Leucocyanidol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**nitric oxide** production and endothelium-dependent vasorelaxation induced by wine **polyphenols** in rat aorta)

L41 ANSWER 24 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:103961 HCAPLUS
DOCUMENT NUMBER: 126:139723
TITLE: Role of **nitric oxide** in gastro-intestinal effects of quercetin
AUTHOR(S): Di Carlo, G.; Izzo, A. A.; Borrelli, F.; Pinto, L.; Perilli, S.; Capasso, F.
CORPORATE SOURCE: Department of Experimental Pharmacology, University of Naples "Federico II", Naples, 80131, Italy
SOURCE: Phytotherapy Research (**1996**), 10(Suppl. 1), S114-S115
CODEN: PHYREH; ISSN: 0951-418X
PUBLISHER: Wiley
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of quercetin on gastro-intestinal transit and fluid accumulation was tested in animals pretreated with NG-nitro-**L-arginine** Me ester (L-NAME) and NG-monomethyl-**L-arginine** (L-NMMA), two inhibitors of **nitric oxide** (NO) synthase, or **L**-

arginine (60 mg/kg), a natural substrate of NO synthase. L-NAME (1 mg/kg i.p.) and L-NMMA (10 mg/kg i.p.), but not D-NAME (1 mg/kg i.p.), potentiated quercetin-induced reduction of gastro-intestinal transit and fluid accumulation in animals treated with castor oil while they had no effect in control animals. These effects were antagonized by **L-arginine** (60 mg/kg i.p.). These results suggest that NO could be involved in quercetin-induced gastro-intestinal effects.

IT **117-39-5**, Quercetin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**nitric oxide** role in gastro-intestinal effects of quercetin)
RN 117-39-5 HCAPLUS
CN 4H-1-Benzopyran-4-one, 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy- (9CI) (CA INDEX NAME)



IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**nitric oxide** role in gastro-intestinal effects of quercetin)
RN 10102-43-9 HCAPLUS
CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

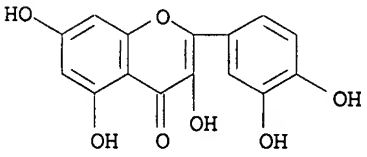
CC 1-9 (Pharmacology)
ST **nitric oxide** gastrointestinal tract quercetin antidiarrheal
IT Antidiarrheals
Digestive tract
(**nitric oxide** role in gastro-intestinal effects of quercetin)
IT **117-39-5**, Quercetin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**nitric oxide** role in gastro-intestinal effects of quercetin)
IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**nitric oxide** role in gastro-intestinal effects of quercetin)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 25 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:411280 HCAPLUS
DOCUMENT NUMBER: 122:180587
TITLE: Inhibition of constitutive endothelial NO-synthase activity by tannin and quercetin

AUTHOR(S): Chiesi, Michele; Schwaller, Roland
CORPORATE SOURCE: Pharm. Div., Ciba-Geigy Ltd., Basel, 4002, Swed.
SOURCE: Biochemical Pharmacology (**1995**), 49(4), 495-501
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of natural **polyphenols** on three isoforms of NO-synthase was investigated. Among the compds. tested, tannin was the most potent inhibiting endothelial constitutive NO synthase (eNOS) with an IC50 of 2.2 μM. Other NOS isoforms (i.e. neuronal constitutive NOS and smooth muscle inducible NOS) were also inhibited but at much higher concns. (selectivity ratio of approx. 20-30). Quercetin was also an effective but less potent inhibitor of eNOS (IC50 = 220 μM). The kinetics of tannin inhibition were investigated to gather information on the mechanism of action. Tannin did not interfere with the interaction of the enzyme with the co-substrates **L-arginine** and NADPH nor with the cofactor tetrahydrobiopterin. The inhibition level was also independent of free Ca2+ concentration as well as of the presence of high exogenous calmodulin concns.

IT **117-39-5**, Quercetin
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(endothelial NO-synthase activity inhibition by tannin and quercetin)
RN 117-39-5 HCAPLUS
CN 4H-1-Benzopyran-4-one, 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy- (9CI) (CA INDEX NAME)



IT **125978-95-2**, **Nitric oxide synthase**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(isoforms; endothelial NO-synthase activity inhibition by tannin and quercetin)
RN 125978-95-2 HCAPLUS
CN Synthase, nitric oxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
CC 4-3 (Toxicology)
ST **nitric oxide synthase** tannin quercetin endothelium
IT **117-39-5**, Quercetin
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(endothelial NO-synthase activity inhibition by tannin and quercetin)
IT **125978-95-2**, **Nitric oxide synthase**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(isoforms; endothelial NO-synthase activity inhibition by tannin and quercetin)

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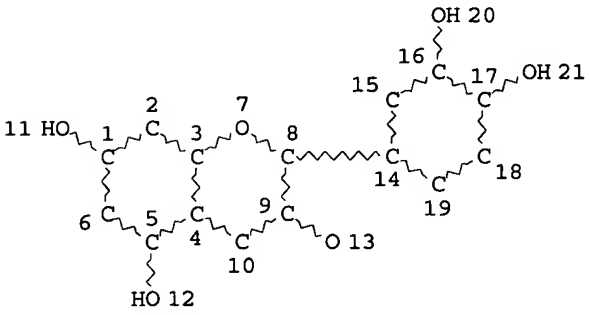


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DEFAULT ECLEVEL IS LIMITED

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L11       123063 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 OR NITRIC(A)OXIDE
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L25          262 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND L21
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L27            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L26 AND L11
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                 OR POLY(A)PHENOL?)
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                 OR L24 OR (L26 OR L27 OR L28) OR L30 OR L34
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                 RY
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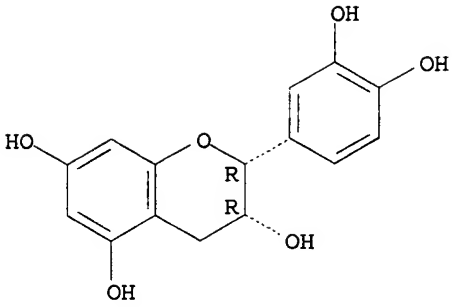
L43 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:963140 HCAPLUS
DOCUMENT NUMBER: 138:395820
TITLE: (-)Epicatechin induces and modulates endothelium-dependent relaxation in isolated rat mesenteric artery rings
AUTHOR(S): Chen, Zhen-Yu; Yao, Xiao-Qiang; Chan, Franky Leung; Lau, Chi-Wai; Huang, Yu
CORPORATE SOURCE: Department of Biochemistry, Chinese University of Hong Kong, Hong Kong, Peop. Rep. China
SOURCE: Acta Pharmacologica Sinica (2002), 23(12), 1188-1192
CODEN: APSCG5; ISSN: 1671-4083
PUBLISHER: Science Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study was aimed to examine the role of endothelial **nitric oxide** in the relaxant response to green tea (-)epicatechin and its modulation of endothelium-mediated relaxation in the isolated rat mesenteric artery rings. Changes in the isometric tension were measured with Grass force-displacement transducers. The (-)epicatechin-induced relaxation was largely dependent on the presence of intact endothelium and was reversed by NG-nitro-**L-arginine** Me ester 10 μmol/L or methylene blue 10 μmol/L, the inhibitors of **nitric oxide** -mediated relaxation. **L-Arginine** at 1 mmol/L antagonized the effect of L-NAME or methylene blue. Pretreatment of endothelium-intact rings with (-)epicatechin 10 μmol/L enhanced the relaxation induced by endothelium-dependent vasodilator, acetylcholine, while this concentration did not influence the endothelium-independent relaxation induced by sodium nitroprusside in the endothelium-denuded artery rings. The results indicate that the endothelium-dependent vasodilation by (-)epicatechin is mainly mediated through **nitric oxide** and low concentration of (-)epicatechin augments endothelium-dependent vasorelaxation in the rat mesenteric arteries.
IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(endothelial; epicatechin induces and modulates endothelium-dependent relaxation in isolated rat mesenteric artery rings)
RN 10102-43-9 HCAPLUS
CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

N═O

IT **490-46-0**, (-)Epicatechin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epicatechin induces and modulates endothelium-dependent relaxation in isolated rat mesenteric artery rings)
RN 490-46-0 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



CC 1-8 (Pharmacology)
ST epicatechin endothelium **nitric oxide** vasodilation green tea
IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(endothelial; epicatechin induces and modulates endothelium-dependent relaxation in isolated rat mesenteric artery rings)
IT **490-46-0**, (-)Epicatechin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epicatechin induces and modulates endothelium-dependent relaxation in isolated rat mesenteric artery rings)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

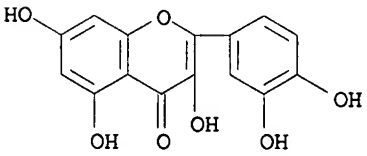
L43 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:883012 HCAPLUS
DOCUMENT NUMBER: 138:395405
TITLE: Quercetin 3,7-dimethyl ether: a vasorelaxant flavonoid isolated from Croton schiedeanus Schlecht
AUTHOR(S): Guerrero, M. F.; Puebla, P.; Carron, R.; Martin, M. L.; San Roman, L.
CORPORATE SOURCE: Laboratorio de Farmacognosia y Farmacologia, Facultad de Farmacia, Universidad de Salamanca, Salamanca, E-37007, Spain
SOURCE: Journal of Pharmacy and Pharmacology (**2002**), 54(10), 1373-1378
CODEN: JPPMAB; ISSN: 0022-3573
PUBLISHER: Pharmaceutical Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The vasorelaxant profile of quercetin 3,7-di-Me ether, a flavonoid isolated from Croton schiedeanus Schlecht (Euphorbiaceae), was assessed in aortic rings isolated from Wistar rats. To gain insight into its structure-activity relation, we compared this substance with quercetin 3,4',7-trimethyl ether (ayanin), another flavonoid isolated from this plant, quercetin 3,3',4',7-tetramethyl ether, a flavonoid synthesized by us, and quercetin. In addition we examined the interaction of quercetin 3,7-di-Me ether with the **nitric oxide** (NO)/cGMP pathway.
According to their pEC50 values (concentration producing a 50% inhibition of the maximal contractile response) to phenylephrine-induced precontraction in rat isolated aorta, the potency order was quercetin 3,7-di-Me ether > quercetin > quercetin 3,4',7-trimethyl ether > quercetin 3,3',4',7-tetramethyl ether (4.70±0.18; 3.96±0.07; 3.64±0.02; 3.11±0.16). The relaxant effect of quercetin 3,7-di-Me ether was significantly decreased by the removal of endothelium as well as by methylene blue, an inhibitor

of guanylyl cyclase, and by NG-nitro-**L-arginine** Me ester hydrochloride (L-NAME), an NO-synthase inhibitor. Therefore, quercetin 3,7-di-Me ether has a NO/cGMP pathway-related profile, with increased vasorelaxant activity due to hydroxylation at positions 3 and 4 of the B ring. In addition, methylation at positions 3 and 7 with respect to quercetin of the C and A rings, resp., seems to further enhance the vasorelaxant activity of quercetin 3,7-di-Me ether.

IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(vasorelaxant flavonoid quercetin di-Me ether from Croton schiedeanus Schlecht)
RN 10102-43-9 HCAPLUS
CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

N═O

IT **117-39-5**, Quercetin
RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(vasorelaxant flavonoid quercetin di-Me ether from Croton schiedeanus Schlecht)
RN 117-39-5 HCAPLUS
CN 4H-1-Benzopyran-4-one, 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy- (9CI) (CA INDEX NAME)



CC 1-3 (Pharmacology)
Section cross-reference(s): 11
IT 7665-99-8, CGMP **10102-43-9**, **Nitric oxide**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(vasorelaxant flavonoid quercetin di-Me ether from Croton schiedeanus Schlecht)
IT **117-39-5**, Quercetin
RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(vasorelaxant flavonoid quercetin di-Me ether from Croton schiedeanus Schlecht)
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:701976 HCAPLUS
DOCUMENT NUMBER: 138:362120
TITLE: Effects of catechins on vascular tone in rat thoracic aorta with endothelium
AUTHOR(S): Sanae, Fujiko; Miyaichi, Yukinori; Kizu, Haruhisa; Hayashi, Hisao
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Department of Medicine, Hokuriku University, Kanazawa, 920-1181, Japan

SOURCE: Life Sciences (2002), 71(21), 2553-2562
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of eight catechin derivs. on vascular tone in rat thoracic aorta were examined Catechin derivs. (10 μM) potentiated the contractile response to phenylephrine in endothelium-intact arteries. The potentiations produced by EGCg and EGC were almost absent in endothelium-denuded arteries and abolished by NG-nitro-L-**arginine** Me ester, an inhibitor of **nitric oxide** synthesis. The catechin derivs. also inhibited endothelium-dependent relaxation in response to acetylcholine. The order of catechin derivs. ranked in terms of both increasing vascular reactivity and impairing endothelium-dependent relaxation was similar; (-)-gallocatechin (GC) ≥ (-)-epigallocatechin (EGC) ≥ (-)-gallocatechin gallate (GCg) ≥ (-)-epigallocatechin gallate (EGCg) ≥ (-)-catechin (C) ≥ (-)-epicatechin (EC) ≥ (-)-catechin gallate (Cg) ≥ (-)-epicatechin gallate (ECg). In addition, EGC inhibited the endothelium-independent relaxation evoked by both sodium nitroprusside and NOC-7, a spontaneous NO releaser, but EGCg inhibited only that by NOC-7. These findings indicate that catechin derivs. produce a potentiation of the contractile response and an inhibition of the vasorelaxant response, probably through inactivation of endothelium-derived **nitric oxide** (NO), and that the hydroxyl on C-5 of the B ring together with the stereoscopic structure between the C-3 group and the B ring of flavanols was of importance in mediating the above effects and that the substitution of a gallate group of C-3 attenuated the effects, probably due to a decreased response to soluble guanylate cyclase in vascular smooth muscle cells.

IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(effects of catechins on vascular tone in rat thoracic aorta with endothelium)

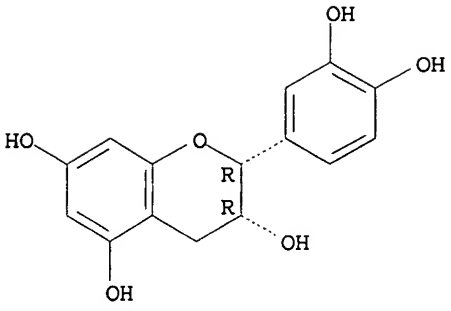
RN 10102-43-9 HCAPLUS
CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

N═O

IT **490-46-0**, (-)-Epicatechin **970-74-1**, (-)-Epigallocatechin **989-51-5**, (-)-Epigallocatechin gallate **1257-08-5 3371-27-5**, (-)-Gallocatechin **4233-96-9**, (-)-Gallocatechin gallate **18829-70-4**, (-)-Catechin **130405-40-2**, (-)-Catechin gallate
RL: PAC (Pharmacological activity); BIOL (Biological study)
(effects of catechins on vascular tone in rat thoracic aorta with endothelium)

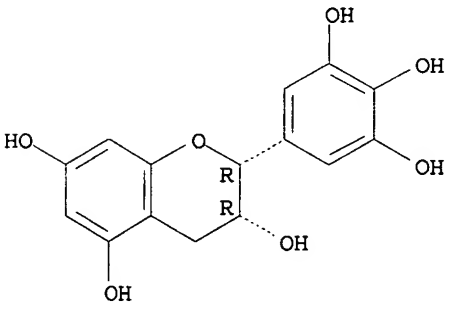
RN 490-46-0 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



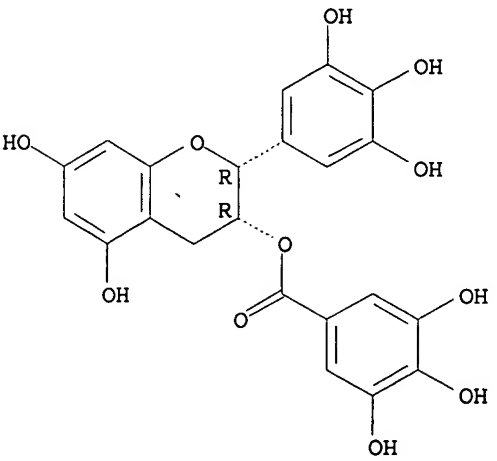
RN 970-74-1 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 3,4-dihydro-2-(3,4,5-trihydroxyphenyl)-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



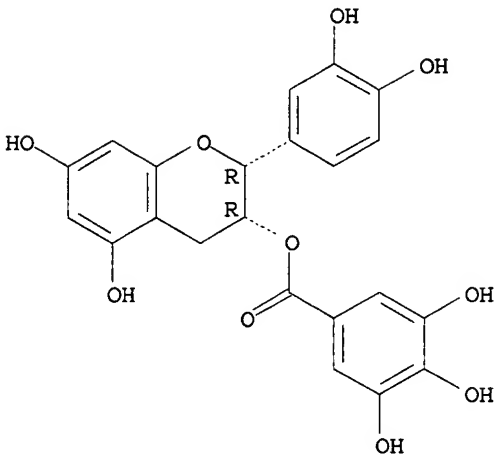
RN 989-51-5 HCAPLUS
CN Benzoic acid, 3,4,5-trihydroxy-, (2R,3R)-3,4-dihydro-5,7-dihydroxy-2-(3,4,5-trihydroxyphenyl)-2H-1-benzopyran-3-ylester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



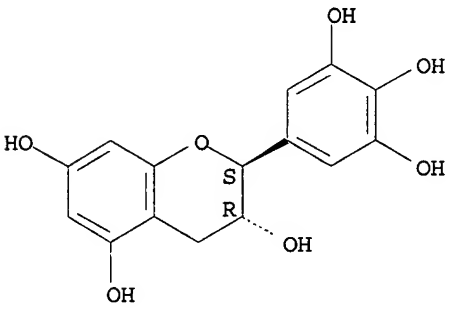
RN 1257-08-5 HCAPLUS
CN Benzoic acid, 3,4,5-trihydroxy-, (2R,3R)-2-(3,4-dihydroxyphenyl)-3,4-dihydro-5,7-dihydroxy-2H-1-benzopyran-3-ylester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



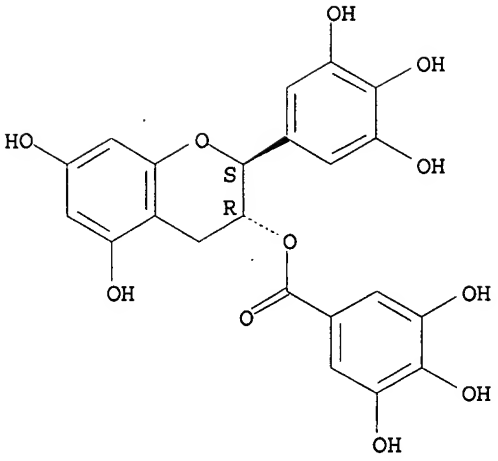
RN 3371-27-5 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 3,4-dihydro-2-(3,4,5-trihydroxyphenyl)-, (2S,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



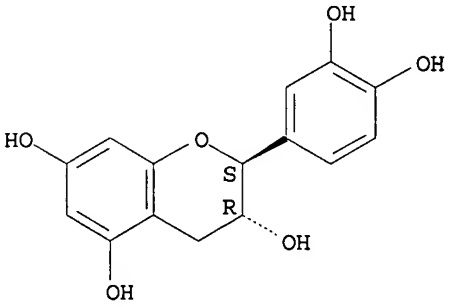
RN 4233-96-9 HCAPLUS
CN Benzoic acid, 3,4,5-trihydroxy-, (2S,3R)-3,4-dihydro-5,7-dihydroxy-2-(3,4,5-trihydroxyphenyl)-2H-1-benzopyran-3-ylester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



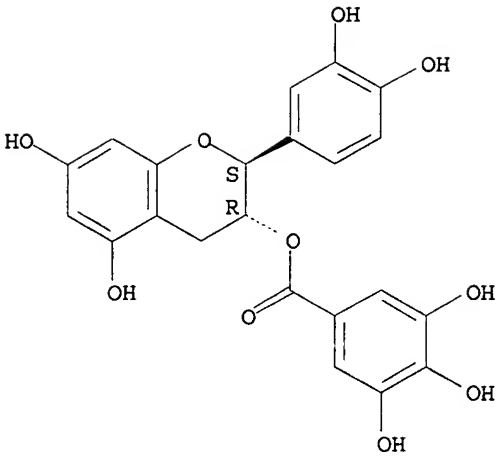
RN 18829-70-4 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-, (2S,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 130405-40-2 HCAPLUS
CN Benzoic acid, 3,4,5-trihydroxy-, (2S,3R)-2-(3,4-dihydroxyphenyl)-3,4-dihydro-5,7-dihydroxy-2H-1-benzopyran-3-ylester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



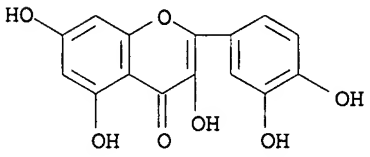
CC 1-3 (Pharmacology)
IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(effects of catechins on vascular tone in rat thoracic aorta with endothelium)
IT **490-46-0**, (-)-Epicatechin **970-74-1**, (-)-Epigallocatechin **989-51-5**, (-)-Epigallocatechin gallate **1257-08-5 3371-27-5**, (-)-Gallocatechin **4233-96-9**, (-)-Gallocatechin gallate **18829-70-4**, (-)-Catechin **130405-40-2**, (-)-Catechin gallate
RL: PAC (Pharmacological activity); BIOL (Biological study)
(effects of catechins on vascular tone in rat thoracic aorta with endothelium)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:711607 HCAPLUS
DOCUMENT NUMBER: 136:5234
TITLE: Dietary polyunsaturated fatty acid and antioxidant modulation of vascular dysfunction in the spontaneously hypertensive rat
AUTHOR(S): Abeywardena, M. Y.; Head, R. J.
CORPORATE SOURCE: Health Sciences and Nutrition, CSIRO, Adelaide, 5000, Australia
SOURCE: Prostaglandins, Leukotrienes and Essential Fatty Acids (2001), 65(2), 91-97
CODEN: PLEAEU; ISSN: 0952-3278
PUBLISHER: Churchill Livingstone
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two currently available edible oils-olive and canola-and two oil blends of plant origin having different n-3/n-6 polyunsatd. fatty acid (PUFA) ratios were evaluated for their ability to modify vascular dysfunction in the spontaneously hypertensive rat (SHR). Synthetic diets supplemented with test oils (5% weight/weight) were fed for 12 wk, and segments of thoracic aorta used to assess vascular function. Vessels from the SHR displayed a spontaneous constrictor response after the inhibition of endothelial cell **nitric oxide** (NO) with Nω-nitro- **L -arginine** (NOLA). Dietary α-linoleate enrichment led to a reduction ($P < 0.05$) in this abnormality with a dietary n-3/n-6 PUFA ratio of 1.0 (blend-1) yielding the best outcome.

Relaxation to acetylcholine (ACh) was unaffected by dietary lipid supplementation. NOLA treated rings also displayed contractions to ACh that were abolished by indomethacin, thromboxane antagonists SQ29548, picotamide and flavonoids kaempferol and quercetin. In contrast, α-tocopherol, rutin and the lipoxygenase inhibitor esculetin resulted in only partial (30-55%) inhibition, and were ineffective against the NOLA-induced contraction suggesting the operation of different biochem. mechanisms in mediating the spontaneous and Ach-induced contractions. Results implicate plant-based oils and antioxidants as potential modulators of vascular function.

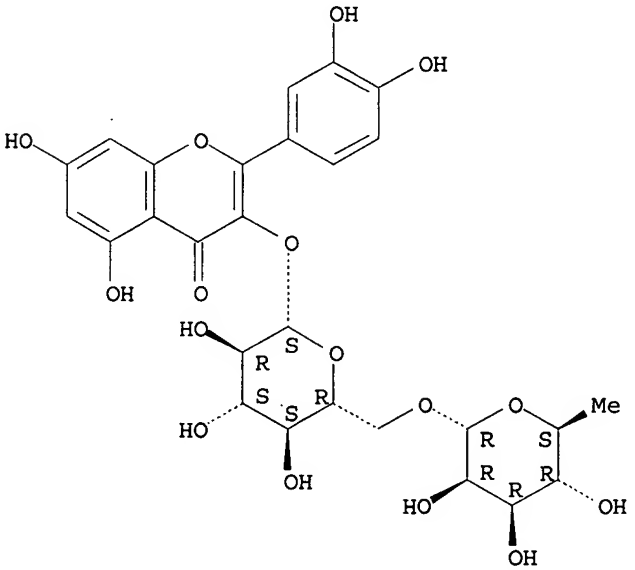
IT **117-39-5**, Quercetin **153-18-4**, Rutin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(polyunsatd. fatty acid and antioxidant modulation of vascular dysfunction in spontaneously hypertensive rat)

RN 117-39-5 HCAPLUS
CN 4H-1-Benzopyran-4-one, 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy- (9CI) (CA INDEX NAME)



RN 153-18-4 HCAPLUS
CN 4H-1-Benzopyran-4-one, 3-[[6-O-(6-deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy]-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



CC 18-5 (Animal Nutrition)
Section cross-reference(s): 14

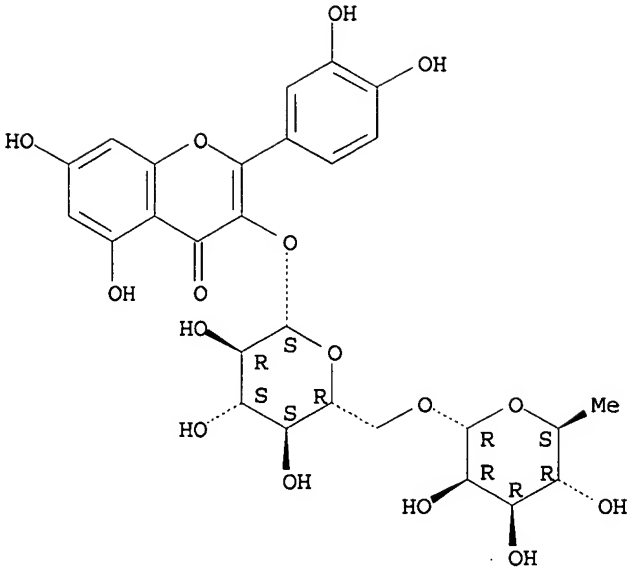
IT 53-86-1, Indomethacin 59-02-9, α-Tocopherol **117-39-5**, Quercetin **153-18-4**, Rutin 305-01-1, Esculetin 520-18-3, Kaempferol 32828-81-2, Picotamide 78712-43-3, OKY046 98672-91-4, SQ29548
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(polyunsatd. fatty acid and antioxidant modulation of vascular dysfunction in spontaneously hypertensive rat)
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:412533 HCAPLUS
DOCUMENT NUMBER: 133:129710
TITLE: Procyanidins in Crataegus extract evoke endothelium-dependent vasorelaxation in rat aorta
AUTHOR(S): Kim, Soon Hoe; Kang, Keon Wook; Kim, Kye Won; Kim, Nak Doo
CORPORATE SOURCE: College of Pharmacy, Seoul National University, Seoul, 151-742, S. Korea
SOURCE: Life Sciences (2000), 67(2), 121-131
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The extract of Crataegus, a mixture of flavonoids and procyanidins extracted from hawthorn, Crataegus oxyacantha, L. and C. monogyna Jacq., relaxed vascular tone or increased production of cyclic GMP in the rat aorta, but flavonoid components of Crataegus extract, hyperoside, rutin and vitexin, did not affect the vascular tone. The aim of the present study was to characterize the endothelium-dependent relaxation elicited by procyanidins fractionated from Crataegus extract in isolated rat aorta. Procyanidins caused endothelium-dependent relaxation which was associated with the production of cyclic GMP. Both responses to these procyanidins were inhibited by methylene blue or NG-nitro-**L-arginine**, but not by indomethacin. Relaxation in response to procyanidins was not affected by atropine, diphenhydramine, [D-Pro2,D-Trp7,9]substance P, propranolol, nifedipine, verapamil and glibenclamide, but were markedly reduced by tetraethylammonium. These findings showed that procyanidins in Crataegus extract may be responsible for the endothelium-dependent **nitric oxide**-mediated relaxation in isolated rat aorta, possibly via activation of tetraethylammonium-sensitive K+ channels.
IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(endothelium-dependent vasorelaxation evoked in rat aorta by procyanidins from Crataegus extract)
RN 10102-43-9 HCAPLUS
CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

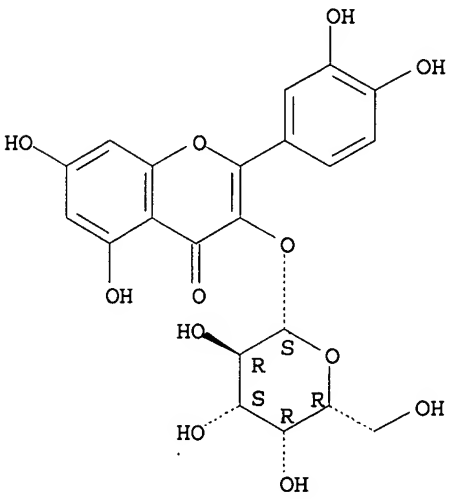
IT **153-18-4**, Rutin **482-36-0**, Hyperoside
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(endothelium-dependent vasorelaxation evoked in rat aorta by procyanidins from Crataegus extract)
RN 153-18-4 HCAPLUS
CN 4H-1-Benzopyran-4-one, 3-[[6-O-(6-deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy]-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 482-36-0 HCAPLUS
CN 4H-1-Benzopyran-4-one, 2-(3,4-dihydroxyphenyl)-3-β-D-galactopyranosyloxy)-5,7-dihydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 1-8 (Pharmacology)
Section cross-reference(s): 2, 11
IT 7665-99-8, Cyclic GMP **10102-43-9**, **Nitric oxide**, biological studies 14127-61-8, Calcium ion, biological studies 24203-36-9, Potassium ion, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(endothelium-dependent vasorelaxation evoked in rat aorta by procyanidins from Crataegus extract)
IT 51-55-8, Atropine, biological studies 52-53-9, Verapamil 58-73-1, Diphenhydramine 66-40-0, Tetraethylammonium **153-18-4**, Rutin **482-36-0**, Hyperoside 525-66-6, Propranolol 3681-93-4, Vitexin 10238-21-8, Glibenclamide 21829-25-4, Nifedipine 80434-86-2, [D-Pro2,D-Trp7,9] Substance P

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(endothelium-dependent vasorelaxation evoked in rat aorta by procyanidins from Crataegus extract)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

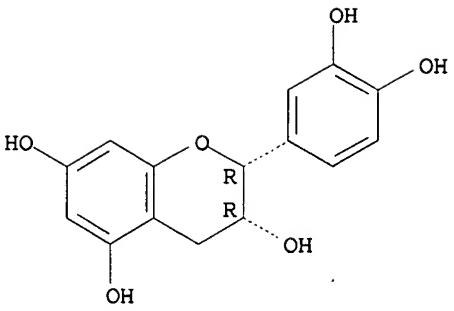
L43 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:262715 HCAPLUS
DOCUMENT NUMBER: 131:82780
TITLE: Involvement of endothelium/**nitric oxide** in vasorelaxation induced by purified green tea (-)epicatechin
AUTHOR(S): Huang, Yu; Chan, Nickie Wai Kei; Lau, Chi Wai; Yao, Xiao Qiang; Chan, Franky Leung; Chen, Zhen Yu
CORPORATE SOURCE: Chinese University of Hong Kong, Department of Physiology, Faculty of Medicine, Shatin, Hong Kong
SOURCE: Biochimica et Biophysica Acta, General Subjects (**1999**), 1427(2), 322-328
CODEN: BBGSB3; ISSN: 0304-4165
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present study investigated the involvement of endothelial **nitric oxide** in relaxation induced by purified green tea (-)epicatechin in rat isolated mesenteric arteries. (-)Epicatechin caused both endothelium-dependent and -independent relaxation. NG-Nitro-**l-arginine** Me ester (l-NAME, 100 μM) and methylene blue (10 μM) significantly attenuated (-)epicatechin-induced relaxation in endothelium-intact tissues. **L-Arginine** (1 mM) partially antagonized the effect of l-NAME. (-)Epicatechin-induced relaxation was inhibited by Rp-guanosine 3',5'-cyclic monophosphothioate triethylamine. In contrast, indomethacin and glibenclamide had no effect. (-)Epicatechin (100 μM) significantly increased the tissue content of cyclic GMP and NG-nitro-l-**arginine** (100 μM) or removal of the endothelium abolished this increase. (-)Epicatechin (100 μM) induced an increase in intracellular Ca2+ levels in cultured human umbilical vein endothelial cells. Iberiotoxin at 100 nM attenuated (-)epicatechin-induced relaxation in endothelium-intact arteries and this effect was absent in the presence of 100 μM l-NAME. In summary, (-)epicatechin-induced endothelium-dependent relaxation is primarily mediated by **nitric oxide** and partially through **nitric oxide**-dependent activation of iberiotoxin-sensitive K+ channels. In addition, there may be a causal link between increased Ca2+ levels and **nitric oxide** release in response to (-)epicatechin.

IT **490-46-0**, (-)Epicatechin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(endothelium-dependent NO-mediated vasorelaxation induced by purified green tea (-)epicatechin)

RN 490-46-0 HCAPLUS
CN 2H-1-Benzopyran-3,5,7-triol, 2-(3,4-dihydroxyphenyl)-3,4-dihydro-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(endothelium-dependent NO-mediated vasorelaxation induced by purified green tea (-)epicatechin)
RN 10102-43-9 HCAPLUS
CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

N═O

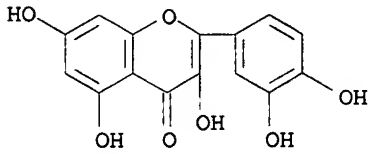
CC 1-8 (Pharmacology)
Section cross-reference(s): 18
ST endothelium vasodilator **nitric oxide** green tea; epicatechin NO muscle relaxant potassium channel
IT **490-46-0**, (-)Epicatechin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(endothelium-dependent NO-mediated vasorelaxation induced by purified green tea (-)epicatechin)
IT **10102-43-9**, **Nitric oxide**, biological studies 14127-61-8, Calcium ion, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(endothelium-dependent NO-mediated vasorelaxation induced by purified green tea (-)epicatechin)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:646677 HCAPLUS
DOCUMENT NUMBER: 119:246677
TITLE: Endothelium-dependent vasorelaxing activity of wine and other grape products
AUTHOR(S): Fitzpatrick, David F.; Hirschfield, Steven L.; Coffey, Ronald G.
CORPORATE SOURCE: Coll. Med., Univ. South Florida, Tampa, FL, 33612-4799, USA
SOURCE: American Journal of Physiology (**1993**), 265(2, Pt. 2), H774-H778
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Current interest in the presumed benefits of wine in protecting against coronary heart disease prompted the authors to investigate possible effects of various grape products on vascular function in vitro. Certain wines, grape juices, and grape skin exts. relaxed precontracted smooth muscle of intact rat aortic rings but had no

effect on aortas in which the endothelium had been removed. Quercetin and tannic acid, compds. known to be present in grape skins, also produced endothelium-dependent relaxation; two other grape skin compds., resveratrol and malvidin, did not relax the rings. Phenylephrine-induced contractions were attenuated by prior exposure of aortic rings to grape skin exts. The exts. also increased guanosine 3',5'-cyclic monophosphate (cGMP) levels in intact vascular tissue, and both relaxation and the increase in cGMP were reversed by NG-monomethyl-**L-arginine** and NG-nitro-**L-arginine**, competitive inhibitors of the synthesis of the endothelium-derived relaxing factor, **nitric oxide** (NO). The vasorelaxation induced by grape products therefore appears to be mediated by the NO-cGMP pathway. If such responses occur in vivo, they could conceivably help to maintain a patent coronary artery and thereby possibly contribute to a reduced incidence of coronary heart disease.

IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BIOL (Biological study)
(vasodilation effect of grape products in relation to aorta guanosine 3',5'-cyclic monophosphate and)
RN 10102-43-9 HCAPLUS
CN Nitrogen oxide (NO) (8CI, 9CI) (CA INDEX NAME)

IT **117-39-5**, Quercetin
RL: PRP (Properties)
(vasodilation effect of, dietary grape products in relation to)
RN 117-39-5 HCAPLUS
CN 4H-1-Benzopyran-4-one, 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy- (9CI) (CA INDEX NAME)



CC 13-6 (Mammalian Biochemistry)
Section cross-reference(s): 1
IT **10102-43-9**, **Nitric oxide**, biological studies
RL: BIOL (Biological study)
(vasodilation effect of grape products in relation to aorta guanosine 3',5'-cyclic monophosphate and)
IT 7665-99-8, Guanosine 3',5'-cyclic monophosphate
RL: BIOL (Biological study)
(vasodilation effect of grape products in relation to aorta **nitric oxide** and)
IT **117-39-5**, Quercetin
RL: PRP (Properties)
(vasodilation effect of, dietary grape products in relation to)

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